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SOME MEDICAL ASPECTS OF OLD AGE



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SOME MEDICAL ASPECTS OF OLD AGE

(BEING THE LINACRE LECTURE, 1922,
ST. JOHN'S COLLEGE, CAMBRIDGE)

OXFORD LIBRARY UNIVERSITY

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PREFACE

THE material in this small volume was collected in connexion with the Linacre Lecture at St. John's College, Cambridge, and has been somewhat expanded since its delivery on 6th May 1922. The introduction is chiefly of local interest in connexion with the history of the Linacre Lecture. Without attempting a complete account of old age and its diseases I have passed in review some ancient and modern medical aspects of this subject, but, except for incidental references, medical treatment has not been considered.

For ready help, especially as regards the illustrations, my cordial thanks are due to C. J. S. Thompson, Esq., M.B.E., of the Wellcome Historical Museum, and for the index I am much indebted to H. M. Barlow, Esq., Assistant Librarian of the Royal College of Physicians of London.

H. R.

CONTENTS

		PAGE
I.	Introduction	1
II.	Duration of Life	9
III.	Onset of Old Age	26
IV.	Factors influencing Longevity	32
V.	Causes of Senescence, with a note on Senescence and Carcinoma	62
VI.	Normal Structural Changes in Old Age	90
VII.	The Physiology of Old Age	115
VIII.	The Description of Old Age in the Twelfth Chapter of Ecclesiastes	129
IX.	Distinction between Healthy and Morbid Old Age	135
X.	Diseases in and of Old Age	139
	Index	157

ILLUSTRATIONS

FIG.		FACE PAGE
1.	William Heberden, M.D., F.R.S.	2
2.	Sir Thomas Watson, Bt., M.D., F.R.S.	4
3.	Professor John Haviland, M.D., F.R.C.P.	6
4.	Henry Jenkins, reputed to have lived 169 years	20
5.	Thomas Parr, reputed to have lived 152 years	22
6.	Katherine, Countess of Desmond, reputed to have lived 140 years	24
7.	Petratsch Zortan, in his reputed 185th year	26
8.	Hungarian husband and wife, reputed to be 172 and 164 years old respectively	36
9.	Sir Henry Pitman, M.D., F.R.C.P., a medical centenarian	52

I

INTRODUCTION

THE Linacre Foundation dating from 1524 is the oldest medical Lectureship in the University, for it was sixteen years later that the Regius Professorship of Physic was established by Henry VIII. Formerly this College Lectureship was held more or less indefinitely by Fellows of the College, with two eminent exceptions, namely, Sir George Paget and Dr. J. B. Bradbury; but in 1908 the Lectureship was made an annual and open appointment, and until this year no member of the College has held this office : I am therefore most deeply conscious of the high honour that has been conferred upon me.

Though the statute that the Lecturer should explain Galen's treatises *De Sanitate Tuenda* and *De Methodo Medendi* as translated by Linacre, or *De Elementis et Simplicibus*, has long lapsed, his first words should be directed to

the pious memory of the founder ; but as in 1908 the late Sir William Osler [1] devoted the first of the new series of Linacre Lectures to a sympathetic consideration of his brother scholar-physician, it would be worse than unwise to attempt more than the briefest reference.

Thomas Linacre (1460–1524) was born at Canterbury of parents who have eluded research, and his connexion with the old family that took its name (Linacre = flax farmer) from a hamlet near Chesterfield in Derbyshire was regarded by J. F. Payne as merely an assumption. Believing that those devoted to learning should be free from the obligations of the married state Linacre remained single, so that he had no direct descendants ; his will [2] contains references to his brother, who had the same Christian name—Thomas—as himself, two sisters Alice and Joan, two nieces Agnes and Margaret, and two cousins Robert Wright of Chester and Richard Wright ; but according to Payne [3] the family history cannot be traced any further. I recently had a faint hope that

[1] *Thomas Linacre*, Linacre Lecture, 1908, St. John's College, Cambridge, by William Osler, M.D., F.R.S., Cambridge University Press, 1908.

[2] *Life of Thomas Linacre*, by John Noble Johnson, M.D., p. 344, 1835.

[3] *De Temperamentis, Galeni Pergamensis*, etc. (translated by Thomas Linacre), by J. F. Payne, p. 5, Cambridge, 1881.



FIG. 1.—William Heberden, M.D., F.R.S., in his 86th year. Linacre Lecturer, 1734–38.

From an engraving by James Ward of a portrait painted by Sir William Beeching, R.A.

I had got on the track of collateral descendants, but on enquiry it was courteously made clear that though the family in question was descended from a Mrs. Linnecar, her connexion with T. Linacre rested on tradition only and that no documentary evidence or genealogical tree existed to justify any claim. It may be remembered that Linacre was one of the earliest English students (*circa* 1488), more than a century before William Harvey, to study medicine and take the doctorate at the ancient University of Padua, which celebrated its seven-hundredth anniversary in May 1922. It is, next, natural to look back to the first holder of this Lectureship, and to wonder what manner of man he was and what he taught. To the Master of St. John's College I am indebted for the few details that are known of Christopher Jackson (B.A. 1524–25, M.A. 1527), who was buried in the old Chapel on July 2, 1528, his death according to a brass erected to his memory in the new antechapel being "e sudore britañico."[1] Some of the Lecturers were without a medical qualification, and of these Matthew Prior (1664–1721), the

[1] The fourth of the five epidemics of the remarkable disease the English Sweating Sickness between 1486 and 1551 occurred in 1528–1529, and is regarded by Dr. F. G. Crookshank as influenza [*Proc. Roy. Soc. Med.*, 1922, xv. (Sect. Hist. Med.) 27].

poet and diplomatist, who was a "Medical Fellow" for life and Linacre Lecturer from July 5, 1706, to July 7, 1710, was the most famous. That he ever lectured is more than doubtful, but he appears to have thought out reasons for not doing so: at any rate his *Alma or the Progress of the Mind* (written about 1715) contains in its third canto the lines:

> how could I explain
> The various labyrinths of the brain!
> Surprise my readers whilst I tell them
> Of cerebrum and cerebellum!
> How could I play the commentator
> On dura and on pia mater!

Three of the Linacre Lecturers under the old dispensation stand out for special remembrance on account of their influence on Medicine:

William Heberden the Elder (1710–1801), the author of the *Commentarii de Morborum Historia et Curatione*, published posthumously (1802), held office from 1734–38, and was described by Sir William Osler as the "English Celsus."[1]

[1] The portrait of Heberden in his 86th year was painted by Sir William Beechey, R.A., who when he got to Windsor found he had forgotten his canvas and sent for a shirt on which he painted the picture, now in the dining-room of the Master's Lodge, St. John's College, Cambridge; there are two copies in the possession of the Heberden family, and one in

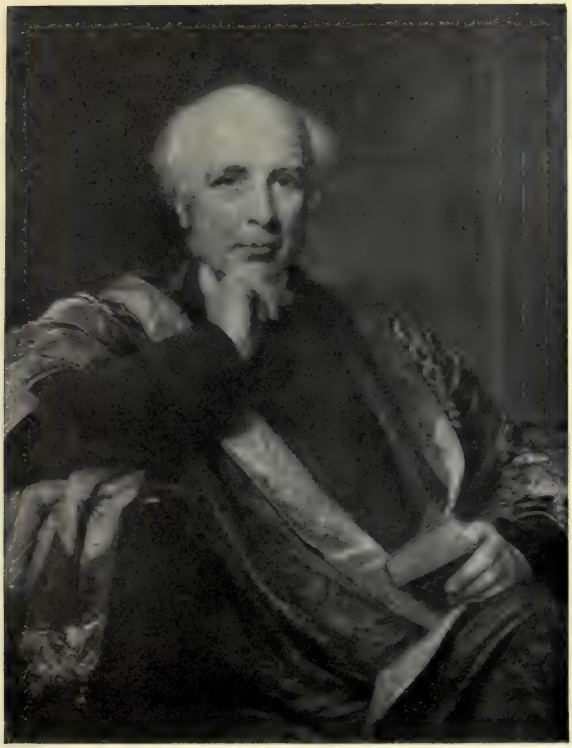


FIG. 2.—Sir Thomas Watson, Bt., M.D., F.R.S. President of the Royal College of Physicians of London, 1862–67. Linacre Lecturer, 1822–26.

From an engraving by George Cousins, R.A., of a portrait painted in 1867 by George Richmond, R.A., now in the Royal College of Physicians of London.

Sir Thomas Watson (1792–1882), whose *Lectures on Physic* held its place longer than any medical text-book of modern times and set an example of style that still commands our admiration and imitation, was Lecturer 1822–26, and in the first year of office was also a Proctor. Subsequently (1862–67), he was President of the Royal College of Physicians of London, the most magnificent of Linacre's Foundations ; this appropriate association was shared by William Baronsdale (P.R.C.P. 1589–1600), by Thomas Gisborne, who was President on three separate occasions (1791, 1794, 1796–1804) alternately with his senior Sir George Baker, and by Sir Norman Moore of St. Catherine's College (P.R.C.P. 1918–22), who gave the Linacre Lecture under the new regulations in 1913 on *The Physician in English History*.[1]

John Haviland (1785–1851), the only one of these three who remained in Cambridge, and the only one who did not become a nonagenarian, was Linacre Lecturer for two periods (1817–22, 1826–47), Sir Thomas Watson

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the Censors' room of the Royal College of Physicians. For some of this information I am indebted to Mr. W. B. Heberden and to Mr. W. Fleming, Bedell of the Royal College of Physicians of London.

[1] The Cambridge University Press, 1913.

intervening. As Professor of Anatomy (not human anatomy) from 1814–17 he delivered the first regular course of lectures on human anatomy ; and when he succeeded Sir Isaac Pennington (also Linacre Lecturer, 1767–1816) as Regius Professor of Physic (1817–51) he was the first to give courses in pathology and the practice of medicine, thus rousing the post from the sleep of a sinecure, and to make the medical examinations a real and rigid test instead of little more than a farcical form consisting of a few *viva voce* questions. Further, had it not been for his influence and insistence the medical faculty might have been abolished, and it was said [1] after his death that the subsequent success of the medical school was due to his exertions. He wrote little and perhaps for that reason his name is seldom mentioned now, but if the work that has since been done by this medical school be his monument he could hardly have a greater.

The somewhat neglected subject of Old Age has a very pertinent connexion with the most essential aim of medicine as a whole, namely, the prevention of disease. For when the ideal of the prophylaxis of infection and of other causes of morbid action is attained, a healthy

[1] *Vide Gentleman's Magazine*, 1851, N.S., xxxv. part i. 205.

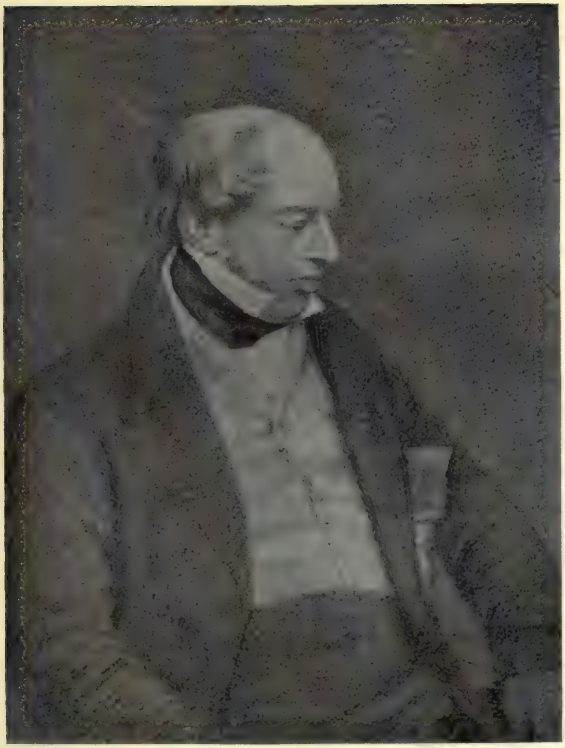


FIG. 3.—John Haviland, M.D., F.R.C.P. Professor of Anatomy, 1814–17, Regius Professor of Physic in the University of Cambridge, 1817–51; Linacre Lecturer, 1817–22 and 1826–47.

From a drawing done in 1851 by Wageman. For this I am indebted to H. A. Haviland, M.B.

old age and physiological death without attendant disabilities and horrors should be the common lot of man instead of being somewhat exceptional in the case of the first and extremely rare as regards the final act. The conditions favouring longevity and *mens sana in corpore sano* are those necessary to make the future of the human race a happy and beneficent prospect instead of a problem inspiring doubt if not pessimism; or in Descartes' words, "we might be free of an infinity of maladies both of body and mind, and even of the infirmities of old age, if we had sufficient knowledges of their causes and remedies." But in addition to this broad ground of interest there are reasons why a discussion of this subject has a special claim for consideration in Cambridge. The objects of a University include the preparation of its alumni for life in its fullest and best sense, and from this point of view the permanent ornaments of the community ever set an unobtrusive example of the way to deserve and enjoy a healthy, happy, and useful old age, namely, activity of mind and body and moderation in all things; such a life of 75 years (that of Professor G. D. Liveing) in the University must be in your recollection as described by the Public Orator

as *tam honesta, tam utilis*. Further, as in private duty bound, I cannot forget that Sir George Humphry, to whom this great medical school owes so much, greatly interested himself in the subject of old age and published the results of an elaborate collective investigation. Lastly, it is desirable that the problems of old age should be attacked by young and active minds in the laboratories of the University and not left as a semi-personal field of enquiry and observation to those whose "way of life is fall'n into the sere, the yellow leaf," and who hear old age's stealthy footsteps catching them up in the race; for in the past most of the writers on geriatrics have written with at least some personal qualification and interest, such as Cornaro, Sir John Sinclair, Sir Anthony Carlisle, Charcot, Sir George Humphry, Sir Hermann Weber, R. Saundby, Metchnikoff, Stanley Hall. As an exception, however, we may point to Dr. John Smith,[1] who, in his thirty-fifth year, was the author of *King Solomon's Portraicture of Old Age*, which paraphrases in 266 pages the "six former" verses of the 12th Chapter of Ecclesiastes containing 205 words.

[1] Γηροκομία βασιλική or *The Pourtract of Old Age wherein is contained a Sacred Anatomy, both of Soul and Body, and a Perfect Account of the Infirmities of Age Incident to them Both*, by John Smith, M.D., London, 1665.

II

DURATION OF LIFE

In the protozoa and some other lowly forms of animal life multiplication by binary fission occurs indefinitely, so that one organism is succeeded by two, and as there is no vestige of a corpse, as Weissmann expressed it, the organism is immortal. Maupas's[1] investigations indicated that without occasional conjugation of two individual protozoa and the resulting rejuvenation the organisms undergo senile degeneration and die ; but Woodruff[2] has shown by observations extending over 13½ years that *Paramoecium*, and so presumably infusoria in general, can multiply indefinitely in favourable conditions without conjugation, though periodically an internal reorganization (endomixis[3]) of the individual takes place. It

[1] Maupas, *Arch. de zool. expér.*, 1899.

[2] Woodruff, L. L., *Proc. Nat. Acad. Sc.*, Washington, D.C., 1921, vii. 43.

[3] Woodruff and Erdmann, *Proc. Soc. Exper. Zool.*, N.Y., 1913–14, xi. 73.

seems not improbable that endomixis provides the rejuvenation otherwise resulting from conjugation. C. M. Child[1] brings forward reasons for modification of the explanation that death is escaped simply by division ; he shows that in certain circumstances senescence occurs in the protozoa as it does in the higher animals, but that death is avoided by the rejuvenescence in each process of reproduction, reconstitution occurring and new organs being formed in the place of the old. In other words, all organisms from the protozoa to man undergo senescence and die unless rejuvenescence intervenes ; this compensation holds good in the lower forms and death may never occur ; but in the higher forms rejuvenescence is so much restricted by the evolutionary increase in the physiological stability of the protoplasmic substratum and the resulting higher degree of individuation that senescence is much more continuous and death is inevitable. It is the penalty for high individuation, and is the result of conditions and processes that have produced the complicated mechanism of the higher animals and man. While holding out the faint hope that the advance of knowledge and of experimental technique may make it possible at some future

[1] Child, C. M., *Senescence and Rejuvenescence*, p. 310, Chicago, 1915.

time to bring about a greater rejuvenescence and retardation of senescence in man and the higher animals, Child points out that the present condition of their protoplasmic substratum is the result of millions of years of evolutionary equilibration, and that this task must therefore be one of extreme difficulty.

Modern biologists such as Driesch, E. Schultz, Child, Steinach, and Julian S. Huxley, to the last of whom I am personally much in debt, have indeed shown that experimentally the life cycle and growth, which are so closely correlated, may be modified dramatically by various methods. By starvation planarian flat worms become smaller and their life cycle is reversed by the process variously called dedifferentiation, reduction, or involution, whereby their structure becomes simpler ; similar retrogressive changes have been produced in the social ascidians, *Clavellina and Perophora* (J. S. Huxley[1]), this process of dedifferentiation or reversible differentiation being the primitive reaction of organisms to unfavourable circumstances. By alternate feeding and starvation Child has kept planarian flat worms at the same size while controls passed through nineteen generations, thus showing that the life of cells

[1] Huxley, J. S., *Journ. Microscop. Sc.*, 1921, lxv. 643.

is not a matter of time but of metabolism. In the higher animals the conditions are of course more complex on account of the self-regulating mechanisms, especially the ductless glands. But by disturbing the endocrine balance experimental biology has produced some remarkable results: by feeding white mice with tethelin (a phospholipin obtained from the anterior lobe of the pituitary) Robertson and Ray [1] found that epithelial proliferation was accelerated, though increase in weight of the animals was retarded, and that the duration of life was prolonged. Drummond and Cannan,[2] however, failed to confirm these results, and feeding with the anterior lobe of the pituitary has given rise to very contradictory reports; acceleration (Clark, Robertson, Goetsch), retardation (Pearl, Wulzen), and no effect (Gudernatsch, Lewis and Miller, Hoskins, Sisson and Broyles [3]) have been described. Steinach's rejuvenation of senile rats by ligature of the vas deferens, which is followed by increase in the interstitial cells of the testis and definite prolongation of life, will be referred to later

[1] Robertson, T. B., and Ray, L. A., *Journ. Chem. Biol.*, 1919, xxxvii. 455.

[2] Drummond and Cannan, *Biochem. Journ.*, Cambridge, 1922, xvi. 53.

[3] Sisson and Broyles, *Johns Hopkins Hosp. Bull.*, Baltimore, 1921, xxxii. 22.

(*vide* p. 76). The retardation of growth due to a diet deficient in vitamins, first proved by Gowland Hopkins[1] in 1912, may be maintained for long periods, but when the diet is appropriately altered growth is resumed and proceeds to the full standard (Osborne and Mendel[2]); it remains to be proved that the total duration of life can thus be prolonged. Though every living species of animal may in normal circumstances have its allotted span of life, this is so subject to accidents and modifications by external influences that the average duration of existence, especially in the long-lived species, does not represent the natural term of years. Thus the expectation of life at birth in England and Wales is 51·5 years for males and 55·35 years for females, as contrasted with the ideal physiological duration of life for 100 years. Violent death in one form or another—traumatic or infective—is so much the rule that the occurrence of natural death in the animal kingdom has been questioned, just as de Candolle denied the natural death of trees and ascribed it to injury or disease. Metchnikoff,[3] who paid special atten-

[1] Hopkins, G., *Journ. Physiol.*, Cambridge, 1912, xliv. 425.

[2] Osborne, T. B., and Mendel, L. B., *Journ. Biol. Chem.*, 1915, xxiii. 439.

[3] Metchnikoff, *The Nature of Man*, English translation, 1903, p. 272.

tion to this question, described natural death in the Ephemerids, day-flies, the imagines of which are incapable of feeding and after an hour or two of " aerial life devoted to love " die, their ova falling into the water ; Sir Ray Lankester accepts the view that they are " wound up " for a few hours only of life, but according to Child death is probably due to starvation. In man natural death from old age—a physiological ending—is very rare, much less frequent indeed than death certificates and ordinary parlance would suggest ; for in such cases there is very commonly some latent disease, such as pneumonia, which just turns the scale in the trembling balance. Montaigne warns us " what an idle conceit it is to expect to die of a decay of strength, which is the last of the effects of the extremest age, and to propose to ourselves no shorter lease of life than that, considering that it is a kind of death of all others the most rare and hardly ever seen." While it must be admitted that this still holds good, it is a stimulus to our efforts to render it no longer true.

The length of days ascribed to Methuselah (969), Adam (930 or, if the " conceit urged by learned men," as Sir Thomas Browne [1]

[1] Browne, T., *Pseudodoxia Epidemica*, p. 396, 6th edition, 1672.

says, that he was 50 or 60 years old when called into being be accepted, 980 years), Seth (912), has aroused attempts at explanation on the basis of a difference in chronology. The suggestion that the "years" were lunar and not solar, in other words containing 30 instead of 365 days, was controverted at length by Eugenius Philalethes[1] (not Thomas, twin of Henry Vaughan "the Silurist") as too radical, for on this interpretation some of the patriarchs would have become fathers of children before they were ten years old. Long ago, Hensler, following Justin, put forward the view that the year consisted of but three months up to the time of Abraham, when it was extended to eight months until the era of Joseph, after which it contained our full complement of twelve months. This explanation was supported by Hufeland[2] on the ground that some eastern nations still reckoned three months to the year. Adopting this explanation Methuselah's age would be cut down to 243 years.

The Psalmist's threescore years and ten and

[1] Eugenius Philalethes, junior, F.R.S., *Long Livers: A curious History of such Persons of both sexes who have liv'd several Ages, and Grown Young again*, 1722, p. 27.

[2] Hufeland, C. W., *The Art of Prolonging Life*, vol. i. p. 121, English translation, 1797.

its sorrowful extension to fourscore are so often exceeded by human beings who appear normal that the possibility of a far longer existence has often been raised. John Sterne or Stearne (1624–69) who, though founder of the Irish College of Physicians, was, according to Mahaffy,[1] more of a theologian than a physician, believed that there was no reason why men should not live as long as the patriarchs before the Flood ; but he also argued that these patriarchal ages must have been exceptional, for had all the human beings between the Creation and the Flood, a period of more than 1400 years, lived to an average breeding age of 400 years and begun, as did the patriarchs, to beget children at the rate of one male every three years, the population of the earth could not have found standing room on its surface ; his colleague in Trinity College, Dublin, Miles Symner, Professor of Mathematics, provided him with a calculation showing that there would have been less than one cubic foot available for each individual. This seems to be echoed in a slightly different connexion by Weissmann's conception of natural death as due to natural selection and as an adaptation

[1] Mahaffy, J. P., *John Stearne*, An Address at the Bicentenary of the Medical School of Trinity College, Dublin, July 1912.

for the good of the species, the degenerated organisms being no longer fertile or useful, an hypothesis hardly necessary, as Metchnikoff points out, when degeneration which is the prelude to dissolution has appeared. Roger Bacon[1] stating that man, originally immortal and after the Fall able to live for a thousand years, had his life gradually abbreviated by corruption of his own making, believed that it should be possible by taking care as to regimen to prolong life for a hundred or more years than the common duration. Since the time of Aristotle the vital cycle has been thought to be a multiple of the period of growth. Francis Lord Bacon considered that animals in general should live eight times as long as they take to come to maturity, and Hufeland,[2] adopting this principle, and regarding 25 years as the termination of adolescence, concluded that man's natural span should be 200 years. Buffon took 14 years as the age of puberty, and multiplying it by 7 decided that human life should naturally be 100 years. Assuming that union of the epiphyses of the long bones marked the time when growth was finally

[1] Bacon, R., *The Cure of Old Age and Preservation of Youth*, p. 63, 1683. Translated by R. Browne.

[2] Hufeland, C. W., *Art of Prolonging Life*, 1797, vol. i. p. 176.

completed, Flourens[1] calculated that throughout the animal kingdom life was five times as long, and that as in man the epiphyses united at 20 or 21 years of age the span of human life should be 100 years.

More modern estimates of the duration of human life under ideal conditions of protection against infection have been to the same effect, thus conforming to the estimate of Cornaro,[2] who died at that age, that a hundred years was "the time allowed to man by God and nature." Metchnikoff,[3] while admitting that there must be variations, considered that man should live more than 100 years, and Luciani fixed the physiological duration of life at 100 years. Ebstein's (1891) estimate of 70 years as the usual duration of life, which is the age at which the maximum number of deaths occur when the first few years of life are excluded, is different from the ideal duration under the best physiological conditions and corresponds more or less with B. W. Richardson's rough rule that the individual's probable age at death can be arrived at by taking the average

[1] Flourens, *De la longévité humaine ou de la quantité de vie sur la globe*, 1856.

[2] Cornaro, L., *Discourses on a Sober and Temperate Life*, p. 101, English translation, 1779, London.

[3] Metchnikoff, *The Nature of Man*, p. 278.

of the ages of his parents and grandparents ; in this procedure the important factor of heredity is taken into account, and the disturbing part played by accidents and infections in modifying the ideal expectation of life is to some extent neutralized by taking the average of the six lives.

Although 100 years may be regarded as the physiological life of man it is rarely reached, and one of several reasons is that the physiological requirements for this apparently exaggerated term of years are very seldom provided. Sir Ray Lankester [1] suggested that just as giants in stature are exceptional variations so centenarians should be regarded in the same light, as giants in years instead of in inches. He meets the obvious objection that whereas the parents of giants are of normal height, longevity and centenarianism appear to run in families, by doubting if the actual quality of potential long life is transmitted and by ascribing family longevity to the inheritance of traditions and habits favourable to long life. In this connexion it should be remembered that many giants are pathological and due to acromegaly, whereas unusual height,

[1] Lankester, E. Ray, *The Advancement of Science*, p. 237, 1890, London.

over six feet, certainly runs in families ; analogy therefore makes it reasonable to believe that length of days, like length in inches, may run in families, although these two approaches to giantism very seldom occur in the same individual.

The authenticity of persons alleged to be of great age rightly excites critical examination, and some of the most famous examples, such as Henry Jenkins (169), Thomas Parr (152¾), Katherine, Countess of Desmond (145), as Sir George Cornewall Lewis and Mr. W. Thom showed, as well as many of the 1712 centenarians in James Easton's [1] list covering the years A.D. 66 to 1799, cannot be regarded as established.[2] In the same category we must place Petrasch Zorten (1537–1724), whose portrait at the reputed age of 185 was reproduced by Sir John Sinclair.[3] Old people take a natural pride in their age and tend to exaggerate it ; according to Mr. G. King [4] the excess in the census returns of persons over

[1] Easton, J., *Human Longevity*, 1799, Salisbury.

[2] The *Observer* of March 26, 1922, contained a note on the discovery of a tombstone in the graveyard of Lamas Street Welsh Congregational Chapel, Carmarthen, recording the death on Nov. 14, 1831, of Ann David, aged 181 years.

[3] Sinclair, J., *The Code of Health and Longevity*, Frontispiece to vol. i., account in vol. ii. p. 274, 1807.

[4] King, G., *Census of England and Wales*, 1911, vol. vii. p. xlvi.



FIG. 4.—Henry Jenkins, reputed to have lived 169 years (1501–1670). Present at Battle of Flodden Field on September 9, 1513.

91 and the deficit in those between 85 and 90 years of age could only be explained by the conclusion that the temptation to overstate the age so as to appear among the nonagenarians had not been resisted. The vast majority of centenarians are naturally among the bulk of the population, namely, the poor, among whom natural selection is provided with a correspondingly greater opportunity of finding those "vigorous frames which promise a long life," and in these circumstances the means of checking the exact age may be less easy than in the case of the well-to-do.

Sex.—Females are more long-lived than males; the 1911 census for England and Wales shows that after 10 years of age there are more females than males living in all the quinquennial periods, the proportion of females progressively increasing until at the age of 85 and upwards there are 645 females to 355 males in 1000 living at that age group. Among centenarians also the ratio of the sexes is much in favour of that popularly said to be the weaker. Out of the 691 reputed centenarian deaths registered in England and Wales during the 10 years 1910–19 inclusive, 504, or 73 per cent, were females, and 187, or 27 per cent, males. But during the same period in

Ireland the disproportion was much less : among the 945 reputed centenarian deaths 545, or 58 per cent, were females, and 400, or 42 per cent, males. It has been said, though without sufficient statistical evidence, that although the female sex is favourable to longevity extreme length of days is attained only by males. The superior longevity of the female sex, in spite of the risks attaching to child-birth, depends on several factors, such as an existence less exposed to accident and infection, a more temperate life, and in addition, so Sir George Humphry argued, on a stronger inherent vitality, for during the first year of life when there is no difference as regards the first two circumstances more boys than girls succumb. The higher male death rate in the first year of life, however, may be partly due to a mechanical cause, namely, the large size of the male infant's head, as a result of which the numerical superiority of male infants born is reduced by the effects of trauma. Another factor is, perhaps, that old women do not feel so old as old men do, and that therefore auto-suggestion plays a less powerful part with them.

The question must arise as to what is the object of the prolongation of life after the

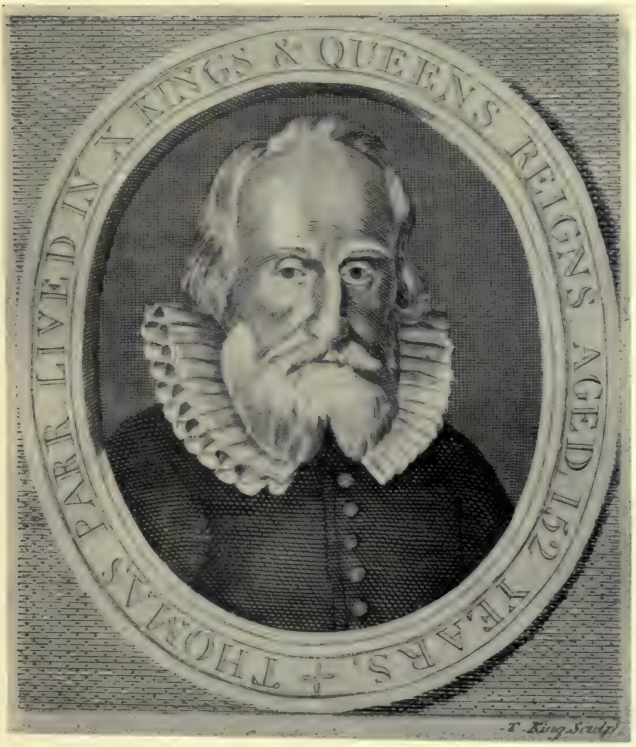


FIG. 5.—Thomas Parr. Reputed to have lived 152 years (1483–1635).
From a Print by Payne.

reproductive function has waned as it does in women—the more long-lived of the sexes—about half-way through the physiological term of years. In some lower animals life terminates very shortly after propagation of the species has been effected; but this is not the rule, and the biological meaning of the continuation of the life of individuals that but cumber the ground and may lead a parasitic existence requires explanation, though educational advantages and moral lessons may undeniably be provided by healthy old age with its store of what a Cambridge man, now justly famous, described in his rather rebellious youth as " that greatly over-rated property experience." It has been suggested by Sir Ray Lankester that the inherent property resulting in longevity may be bound up as a " correlated variation " with some other characteristic useful in the struggle for existence and the perpetuation of the species. An obvious possibility is that the long-lived have a higher fertility rate than average mortals. Hufeland [1] argued that as very old people are nearly always married more than once and generally at a very late period of life " a certain abundance in the power of generation is favourable to longevity." There

[1] Hufeland, C. W., *The Art of Prolonging Life*, 1797, vol. i. p. 168.

are few satisfactory data to determine the converse proposition with which we are now concerned, namely, is longevity accompanied by unusual fertility? As already mentioned, the great majority of centenarians are found among the bulk of the population, namely the poor, who are far more prolific than the well-to-do; but this does not prove much, for the inverse correlation of fertility and good social status is largely artificial and due to voluntary birth control. Among the 824 persons between 80 and 100 years of age analysed by Sir George Humphry[1] in 1889 there were 335 married men and 292 married women, and in each group the average number of children was six, which is somewhat in excess of what is popularly supposed to be the average size of a family; but the question of average fertility is one on which Dr. Major Greenwood warns me that it is difficult to give an unambiguous answer, for it all depends on whether completed or incompleted fertilities are meant; thus in the 1911 census the completed fertilities average 5·8 and the uncompleted 4·2. No value could, he considers, be attached to the general figure obtained by dividing the total number of children by the total number of couples

[1] Humphry, G. M., *Old Age*, p. 126, 1889, Cambridge.

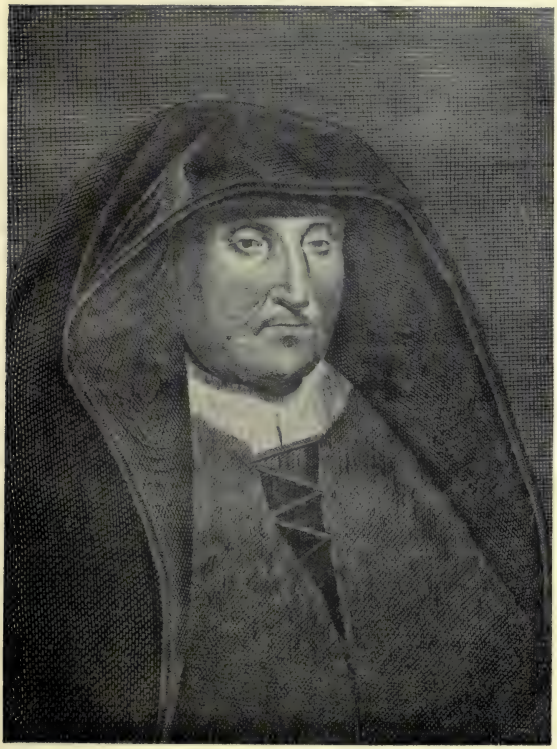


FIG. 6.—Katherine, Countess of Desmond. Died 1604 at reputed age of 140.

enumerated. Hence Sir George Humphry's and other statistics are not really comparable. While finding that longevity was equally shared by the single and married women and by those who had children and by those who were barren, Sir George Humphry stated that among those who had children fertility was associated with longevity.

III

ONSET OF OLD AGE

The onset of old age varies in different countries, and, like the development of puberty, is accelerated by the high temperature of tropical countries. There is also considerable variation in families and individuals of the same race and country ; thus while one man may be senile at 60 years of age another is vigorous both in mind and body at 80. The inconstancy of onset depends on the various factors that may play a causal part ; old age may be a physiological involution, but too often is a pathological product. When the period of reproductive power (maturity) wanes that of old age begins ; in women this is marked by the menopause, the age of 45 years being taken as the limit of fertility, but before this even in the late thirties the spectre of fading attractiveness may upset the matron and lead to the irregularities of the " dangerous age." For man there is no such index, and the change is

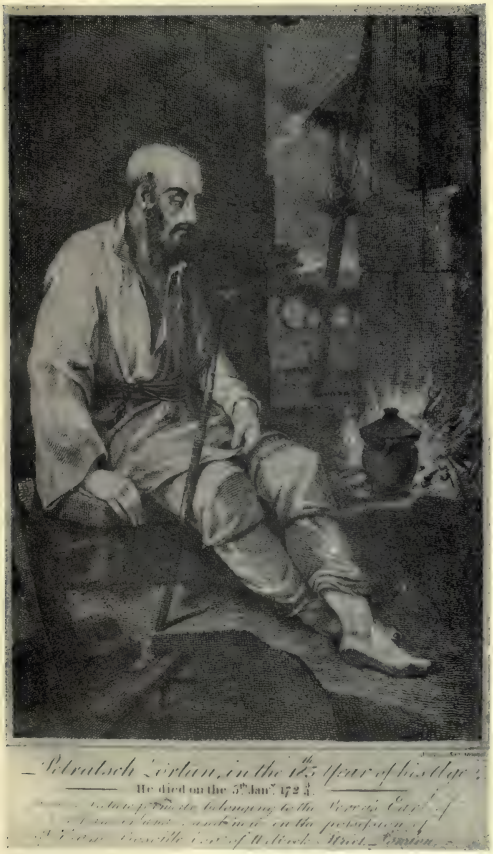


FIG. 7.—Petratsch Zortan, a Hungarian. Reputed to have lived from 1537 to 1724.

so insidious that most of us would expostulate at Stanley Hall's [1] statement that old age in men begins in the early forties and sooner in women, or less than half-way through the physiological lifetime of a hundred years. According to Dante 45 marks the termination of youth, and it seems generally agreed that as a rule—and every one is entitled to consider himself as the exception—

> The gay bloom of fifty passes quickly away
> And people get fat and infirm and all that.

It has from analogy of the female sex been rather fancifully suggested that in man there occurs about the age of fifty a critical period (*climacterium virile*) due to changes in the sex glands (Mendel [2]) or prostate (Rankin [3]) ; but of this there is no proof. It recalls as a kind of echo the ancient conceptions of the grand climacterics at 49 (a multiple of the number 7), 63 (7 × the magical number 9 of the Arabians), and 81, and the description in 1807 by Professor B. Waterhouse [4] of Cambridge, Mass., who in 1800 introduced Jennerian

[1] Hall, G. Stanley, *Senescence : The Last Half of Life*, 1922, London and New York.

[2] Mendel, K., *Neurol. Centralbl.*, 1910, xxix. 1124.

[3] Rankin, G., *Brit. Med. Journ.*, 1919, i. 63.

[4] Waterhouse, B., Letter to Sir John Sinclair in the latter's *Code of Health and Longevity*, 1807, i. 33.

vaccination into America, of a kind of male moulting between 43 and 50 and a worse one at 63, an idea expanded into the climacteric disease imagined in 1813 by Sir Henry Holland.[1] There is indeed no doubt that after an illness, and the so-called climacteric disease admittedly seldom occurred without some previous factor such as an attack of gout, a common cold, a bout of intemperance, recent marriage, or particularly grief or bereavement, old age may come on apace. In some instances the so-called climacteric disease was perhaps really chronic renal disease, in others merely the prolonged or imperfect convalescence due to some lingering infection after an acute illness, such as influenza ; and, as in the latter case recovery may occur, Holland's contention that recovery was an argument in favour of the existence of this climacteric disease holds good only in distinguishing it from permanent senility, which indeed was the objection that he was concerned to meet. The conception of the climacteric disease is interesting historically only ; and it may be agreed that apart from accidents of environment the progress of senescence in healthy men is gradual and uneventful.

[1] Holland, H., *Med. Trans. Coll. Phys.*, London, 1813, iv. 316.

So stealthy is the onset of senescence that commonly it is not recognized by its victim and, though he may seldom mention it, every man is firmly convinced that he not only looks but is at least ten years less than the register would tell him. Though unconscious of the change in himself he notes it with perhaps some self-congratulation in his contemporaries. It is only if he tests himself, for example by timing himself for a mile's walk, that a healthy man of say 70 years has it borne in on him that he is not what he was. The information that he is old may be suddenly conveyed by overhearing the chance remarks of others, by catching a reflection of his bent back in a mirror, by tardy recovery from illness, or the advent of some disability, such as hypertrophy of the prostate or dyspnoea on holiday exertion. Perhaps the commonest warning is a feeling of fatigue. Sir Andrew Clark regarded the onset of old age as the period when a man ceased to adjust himself to his environment ; but some persons never are able to do this, and misfits are not necessarily old. Laurentius divided old age beginning at 50 into the three stages of " the green because it is accompanied with prudence, full of experience, and fit to gouerne common weales," the second at 70

years is "very cold and drie," and the last, without a specified age incidence, is that of decrepitude corresponding to the famous description in the 12th chapter of Ecclesiastes. A more modern and comforting division is that of Lacassagne [1] of pre-senility, old age beginning at 60 or sometimes 70 in men, and in women 10 to 15 years earlier, advanced old age, and lastly decrepitude. Nascher [2] speaks of a senile climacteric about the latter part of the 7th or 8th decade—the transitional period between old age and decrepitude—corresponding to the changes at puberty and at the menopause.

Precocious old age due to the effects of disease, especially syphilis and acute infections, and to metabolic defects, which permanently damage the cells of the body, has a special interest as it supports Metchnikoff's pathological view that old age as ordinarily seen is a result of toxic injury (*vide* p. 82). Hastings Gilford [3] has specially investigated premature senility, and under the title progeria has described a remarkable condition of premature senility

[1] Lacassagne, A., *L'Homme vers la fin de sa vie*, p. 7, 1919, Lyon.

[2] Nascher, I. L., *Geriatrics: The Diseases of Old Age and their Treatment*, p. 18, London, 1919.

[3] Gilford, Hastings, *Med.-Chir. Trans.*, London, 1897, lxxx. 17. *Disorders of Postnatal Growth and Development*, 1911.

combined with, or secondary to, infantilism. This condition was independently described in 1910 by Variot and Pironneau [1] as the senile type of nanism. In such cases it would appear reasonable to ascribe these two opposite conditions to the same toxic or other factor, the infantilism depending more on damage to the ductless glands before development was complete, and the senile changes to direct injury of the cells in the body in general.

[1] Variot et Pironneau, *Bull. Soc. pédiat. de Paris*, 1910, xii. 307.

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IV

FACTORS INFLUENCING LONGEVITY

The determining factors of long life may be broadly divided into those included under heredity, environment, due functional activity, and personal habits. It is impossible to separate these factors into watertight compartments, for a certain amount of overlapping between them is unavoidable.

Heredity

The influence of heredity has often been insisted upon and is perhaps the most important factor in longevity. Out of 824 persons between 80 and 100 years of age analysed by Humphry, 406, or 49·4 per cent, came of long-lived families. Numerous striking examples of such families are on record, but a few only need be given. Roy[1] quotes the case of Dr. Iverex, who died in 1700 at the age of 104,

[1] Roy, D., *Thèse de Paris*, No. 110, 1910.

his father at 112, his mother 107, and his grandfather 130 years, and gives four other examples of three centenarians in the same family. Another remarkable family group was that of Joseph Retas who died at Tarbes at the age of 118 in 1888, and was the son of a man aged 111 years and had a brother aged 114 years. Two centenarian twin sisters were recorded in a village near Athlone[1]; centenarian sisters and brothers are not so very exceptional. Sir Hermann Weber[2] recorded two families, in one of which the average age of ten children was over 90 years and in the other of eight children nearly 90 years.

A good stock may ensure long life in the face of adverse environment, such as town life and alcoholism; thus Dr. John Brownlee[3] showed statistically that while persons dying at the age of 51 in the average environment would have, had they lived in the country, a mean life of seven years longer, this difference was less at higher ages, and remarks that a person who has the potentiality of living to

[1] *Lancet*, 1889, ii. 349.

[2] Weber, Hermann, *On Longevity and Means for the Prolongation of Life*, 1919, 5th edition, by F. P. Weber, London.

[3] Brownlee, J., *The Use of Death Rates as a Measure of Hygienic Conditions*, p. 51. Special Report Series No. 60. Medical Research Council, 1922.

the age of 80 years has a force of life which is more or less independent of environment. Sir George Savage [1] often noted that of two aged members of the same family one was sober the other intemperate ; and a good many centenarians have taken alcohol in quantities that would be too much for ordinary people.

Heredity is not an all-powerful factor, for an individual whose family history is not remarkable for longevity may greatly prolong his life by carefully correcting unfavourable hereditary tendencies. Thus the late Sir Hermann Weber, who lived to the age of 95 as the result of practising the maxims of his *Prolongation of Life*, mentions that his mother died of cardiac failure before she was 60 and his father at 60 from cerebral haemorrhage, and he gives other instances of the same happy result of wise management. Not unfrequently husband and wife both live to an advanced age, no doubt often as the result of favourable environment. A photograph of a married couple both 101 years old appears as the frontispiece of Sir George Humphry's book on *Old Age*, and must of course be accepted ;

[1] Savage, G., *Memorial to Sir William Osler*, vol. i. p. 247, 1919, New York.

but the same cannot be said of the frontispiece to volume ii. of Sir John Sinclair's *Code of Health and Longevity* (1807), representing the Hungarian husband and wife, aged respectively 172 and 164 years, who had been married 147 years.

It has been suggested that " cell-memory " by providing experience as to the proper way to behave at the different periods of life has a bearing on the coming of old age ; Samuel Butler [1] argued that cells without hereditary memory of past existence at, say, 75 years, would become puzzled and so disordered as to die. Parkes Weber [2] has modified this view by assuming a failure of the wish to live on the part of the nerve cells of the brain, a want which might also be hereditary. The possession by the cells of " the will to live " would be an important factor in longevity and should be obtained by individual effort or in other words be an acquired character, though the reverse conditions such as physical mutilations,[3] often spoken of as acquired characters, are known not to be inherited.

In different countries and in different

[1] Butler, S., *Evolution, Old and New*, p. 380, 1911.

[2] Weber, F. P., *Med. Press*, London, 1920, N.S., cix. 271.

[3] Compare Fischer, Martin H., *The Unpopular Review*, 1919, ix. 323.

individuals the cells of the body may differ in the rate at which they live ; they have, as Sir James Paget [1] said, a different " time-rate " ; in some the time-rate is rapid, for example in the natives of hot climates where maturity comes early and old age at a time that seems very premature by our standard ; in others the body, sometimes the mind, works slowly, is set at a more leisurely rate and therefore takes longer to run its course. In some persons this appears to be shown by a slow pulse, a characteristic that may also be hereditary.

Of the hereditary factors most concerned in longevity the inherent vitality of the central nervous system is the most essential ; physiological death in man and the higher animals is probably due to failure of the cells of the brain, which do not multiply after birth and are less capable of rejuvenescence than those of the other organs. The integrity of the cardio-vascular system is also most important ; in Sir William Osler's [2] words much depends " on the quality of arterial tissue (vital rubber) which the individual has inherited." Accord-

[1] Paget, J., " Errors in the Chronometry of Life," in *Studies of Old Case Books*, p. 92, 1891, London.

[2] Osler and McCrae, *The Principles and Practice of Medicine*, p. 834, 1920, New York and London.



FIG. 8.—John Rovin and Sarah his wife, Hungarians, at their reputed ages of 172 and 164 years respectively; their married life lasted 147 years.

ing to Sir Clifford Allbutt [1] there are two modes of hereditary transmission of arteriosclerosis, the direct and the indirect ; the direct which he calls decrescent or primary, consisting in an original frailty or toxic susceptibility which like other peculiarities may run in families ; and the indirect or hyperpietic, a secondary event due not to inherent taint in the arterial walls but to metabolic changes causing high arterial pressure ; it is in such families with hereditary high blood pressure that cerebral haemorrhage occurs in one generation after another about the same age (65-70). In examining people the discovery of a blood-pressure low for their age often justifies, in the absence of any pathological condition, the suggestion that the family is long-lived. The frequency of cardiac hypertrophy (43 per cent of Councilman's cases), even though it be a pathological condition, shows that its reserve power is good. Death among the aged very commonly depends on some morbid change in the cardio-vascular system ; thus at the Royal Hospital, Chelsea, Majors R. J. C. Thompson and R. E. Todd [2] found that among 169

[1] Clifford Allbutt, *Diseases of the Arteries including Angina Pectoris*, vol. i. pp. 164-7, 1915, London.

[2] *Lancet*, 1922, i. 874.

deaths of pensioners with an average age of 77·2 years the largest number 64, or 38 per cent, were due to this cause ; lesions of the respiratory system, pneumonia, and broncho-pneumonia, coming next with 41 deaths, or 24 per cent, malignant disease being responsible for 22, or 13 per cent. The nervous and circulatory systems are intimately correlated with each other, disorder or disease of one, particularly of the cardio-vascular system, exerting an evil influence on the other. In a negative manner weakness of the digestive system may favour longevity by preventing the excesses which vigorous individuals may for a time at any rate indulge in with impunity ; but as a rule the digestion of the long-lived is good.

The first-born is significantly handicapped, as Karl Pearson [1] has shown, and more subject to tuberculosis, insanity, and criminality. But out of 71 centenarians analysed by Sir George Humphry 17, or 24 per cent, were firstlings, and 24 per cent of 824 persons between 80 and 100 were first-born. It must be remembered that first-born are more numerous than any others, and some of the above were

[1] *On the Handicapping of the First-Born*, Eugenics Lecture Series, x., 1914.

only children. The most frequent position in the family among these 895 old people analysed by Sir George Humphry was the third.

Environment

The influences included under the head of environment are numerous, and this factor cannot be entirely separated from that of heredity, for environment may favour and shape hereditary characteristics. The subject of the harmony and the want of harmony existing between man and his surroundings is so vast that it is possible to touch on a few only of these aspects.

The average length of life varies in different countries ; a temperate or moderately cold climate is conducive to a slower development of maturity and so to a longer life than tropical regions. The Balkans, Greece, Scandinavia, the Pyrenees, California, and small islands are considered favourable to longevity. A high elevation has been regarded as an important factor, and the great age of the monks of Mount Athos has been thus explained, though other influences, such as simplicity of life, may well play a part. Switzerland, however, does not conform to the view that a high elevation

confers long life on its inhabitants. From observations around Dijon Noirot[1] drew up a scale showing that the elevation above the sea and length of life rose together. National habits have a bearing, and this may help to explain the longevity of the Jews, who follow the Mosaic laws of health, and why the French appear to be more long-lived than the Germans. The long-continued persecution and hard life that the Jews have undergone has led to the survival of the fittest and a hereditary factor. The former simplicity of the Russian peasants would also provide a reason for their reputed longevity (one centenarian in every thousand). In Ireland, though much depleted by migration of young adults, the absolute number of centenarians is very high; in 1888 there were 208 such deaths, or 43 per million living; in the ten years 1911–20 inclusive there were 1030 centenarian deaths, or about 23 per million living; and the Registrar-General, Sir William J. Thompson, kindly informs me that in 1921 there were 314 centenarians living in a population of 4,496,000, or about 70 per million of the population. It seems probable that this is the outcome of a simple life. In England and Wales the number of

[1] Noirot, L., *L'Art de vivre longtemps*, p. 195, 1868, Dijon.

centenarians is both relatively and absolutely less ; in 1887 there were said to be about 2 and the 1911 census returns showed 3·6 living centenarians per million of the population ; the return of the 1921 census is not yet available. In the ten completed years 1910–19 there were 691 centenarian deaths, or an average of 69 annually among a population averaging about 35 millions—about two per million living. In California there are, according to Laurent,[1] 300 centenarians in a population of three millions, or 100 per million, the extremely favourable climatic conditions accounting for this high ratio. In the same country there is a difference, much to the advantage of the rural inhabitants, between the prospect of longevity in the towns and in the sparsely populated districts. From their open-air life agricultural labourers provide the largest percentage of long lives.

Improved Conditions of Life.—There is good evidence that the average expectation of life has improved in this country during the period that increasing attention has been paid to sanitation. This is shown by the tables of the Registrar-General. For most of the following information I am indebted to Dr. T. H. C.

[1] Laurent, O., *Bull. Acad. de méd.*, Paris, 1919, lxxxi. 835.

Stevenson of the General Register Office, Somerset House. In 1838–54 the expectation of males at birth in England and Wales was 39·91 years, in 1901–10 the male and female expectations at birth were 48·53 and 52·38 years respectively, and the latest available expectations at birth (English Life, Table No. 8, Supplement to the Seventy-fifth Annual Report of the Registrar-General, Cd. 7512) are 51·6 for males and 55·35 years for females. But the expectation is probably considerably more now, as the death rates have fallen appreciably since 1910–12. The Prussian male expectation of life at birth has increased from 35·38 years in 1867–77 to 46·43 in 1906–10;[1] and the Swedish[2] expectation of life at birth from 39·5 years in males and 43·6 years in females in 1816–40 to 54·5 and 57 years respectively in 1901–10. In North America[3] there has been a fall in the death rate in every age group in 1920 as compared with 1910.

[1] *Annuaire internationale de statistique*, Part II., Europe, Movement of the Population, Table 12, pp. 180-81.

[2] *Statistiska Meddelanden*, Ser. A., Band I. 1 *Dödlighets- och Lifslangdstabeller for Åren 1816–1910 af Kungl. Statistiska Centralbyrån*, Stockholm, 1912, p. 28. (For this reference I am indebted to Dr. Major Greenwood.)

[3] *Public Health Reports*, Treasury Department, Washington, 1922, xxxvii. 487.

The increased expectation of life has been especially prominent in early and adult life. Examination of the Registrar-General's census returns from 1851 to 1911 show that although there were more persons per million living between the ages of 55 and 75 there were less above the age of 75 at the end than at the beginning of this 60-years' period. It has been suggested that the increased survival in the earlier period of old age is due to the saving of life in infancy and that, as these lives are not prolonged above the age of 75 or so, the diminished proportion of persons living to become octogenarians is explained (H. Weber).

The influence of past diseases is perhaps most conveniently considered in connexion with environment. As infection must necessarily impair the vitality of the cells of the body, either temporarily or permanently, it would be natural to expect that those who live to a great age would show a remarkably clean bill of health. This is often true. But it is at first sight rather disconcerting to find that nearly half of the 824 persons between 80 and 100 years of age analysed by Sir George Humphry had had severe illnesses at one time or another ; many of these, however, were

acute infections. It is noticeable that 85 per cent were free from rheumatism in the hands (selected as a convenient test in his collective investigation), which in the light of present opinion that arthritis is the result of a focal infection would appear to show that these old people are remarkably free from chronic disease. Long-continued infection or intoxication would be a far more potent factor than a transient illness in producing permanent change in the cells. A short acute infection would cause changes in the cells which might, like those of fatigue, be temporary and recoverable. Saundby's[1] dictum may be accepted as fairly accurate, exception being made for peripheral mutilations, namely, that those only can expect to live to extreme old age who at the age of 60 possess bodies free from disease. But critical examination would no doubt show that focal infections become increasingly frequent as the years go on ; this is particularly true as regards oral sepsis ; after two years' experience of 500 pensioners at the Royal Hospital, Chelsea, Thompson and Todd have never seen a tooth in a healthy condition there. It is noteworthy that dental disease seems to have become common with the advent of civilization, as

[1] Saundby, R., *Old Age, Its Care and Treatment*, p. 21, 1913, London.

judged by examination of ancient skulls, though the loss of teeth is an accompaniment of the bony changes in old age, and very old people seldom have more than a few teeth left. On the other hand, an acute illness is often the apparent starting-point of old age ; there may be a long and imperfect convalescence due to persistence of infection, or deterioration may be due to auto- or hetero-suggestion (*vide* p. 48).

The influence of syphilis, whether congenital or acquired, is one of the most important in the prevention of healthy longevity ; it not only directly disables and kills, especially in infancy and in the fifth decade, but it damages the vitality of the cells thus producing degeneration and premature senility, and favours secondary infections.

It is clear that for the preservation of health detection of disease in the earliest stage is all-important, and that this can be attained by periodic examination by a medical man ; but obvious though this may be, the average man waits to call in a doctor until he knows that he is ill. Timely advice as to methods of life, food and drink, occupation, or environment would often prevent disease and premature death. In 1913 the Life Extension Institute was founded in New York for such

periodic examination and report, and the Life Assurance Companies, finding that persons so examined showed, at any rate for some years, a death rate lower than that anticipated, gave it financial support.

Functional Activity

As is well known, disuse leads to atrophy, and biologically conditions rendering an animal's supply of food extremely easy and safe are followed by atrophy of the parts no longer necessary in a state which may thus come to border on parasitism ; in an extreme degree this result is shown in barnacles (degenerated crustaceans) and ascidians (degenerated vertebrates). In man the cessation of an active life on retirement to the country, described by Samuel Johnson as " a kind of mental imprisonment," or the sudden acquisition of wealth, often exerts a most evil influence ; for if the whole body is no longer kept in a condition of functional activity, those parts allowed to remain relatively idle begin to degenerate and atrophy ; loss of function means a diminished blood supply and nutrition, and so degenerative atrophy. According to Laurentius " nothing hastens old age more than idleness." James

Easton,[1] who collected 1712 records of centenarians, many of them open to criticism, endorses Hufeland's dictum that no idler has ever attained to a remarkably great age ; and Sir Thomas Browne's[2] quaint injunction " Dull not away thy days in sloathful supinity and the tediousness of doing nothing " is old but true wisdom.

The axiom that disuse leads to atrophy applies perhaps even more to mental activity, for resting and rusting of the brain slow the pace of the whole body, whereas an alert mind can exist in an infirm body. There is no doubt that occupation with a strong desire to live for the accomplishment of a definite purpose exerts a most beneficial influence, and there have not been wanting some, such as Karl Marx, who have preached that old age is in great part a matter of will. Speaking of the circle in which Madame du Deffand moved Lytton Strachey[3] says " They refused to grow old ; they almost refused to die. Time himself seems to have joined their circle, to have been infected with their politeness, and to have absolved them, to the furthest

[1] Easton, J., *Human Longevity*, p. xxvi, Salisbury, 1799.
[2] Browne, T., *Christian Morals*, Part I. Section XXXIII.
[3] Strachey, L., *Books and Characters*, p. 83, London, 1922.

possible point from the operation of his laws. Voltaire, d'Argental, Moncrif, Hénault, Madame d'Egmont, Madame du Deffand herself all lived to be well over eighty, with the full zest of their activities unimpaired." Want of this joy in life necessarily engenders carelessness and neglect of personal hygiene, and loss of the power to react to the environment. As the years advance and the younger generation come up, the suggestion that "his day is done," that he has had his innings, and that it is time for him to step aside, is made to the senior not only by his family and his juniors —hetero-suggestion—but by himself, and he may then, after the modern fashion, get into the habit of repeating mentally "I am getting older and older every day." A slight illness or incapacity may be magnified into a conviction that the end is near, and as a result of the loss of self-reliance a state of increasing invalidism is established and becomes progressive without any other cause. Just as a fall, an exacerbation of rheumatic pain, a slight operation or indisposition, necessitating rest in bed for a short time, may be followed by a functional loss of power in the lower extremities, so a more general suggestion of failing powers may lead to mental deterioration. Thus too

often a man's last occupation is to shorten his existence and make it miserable. Finot,[1] who rather optimistically believes that man should be able to live 150 years, regards this poisonous auto-suggestion as one of the factors that prevent such an achievement. Observation of contemporaries suffering from premature senile changes, due to pathological factors, may no doubt stimulate this destructive form of auto-suggestion. There is therefore a basis for the idea[2] attributed to the late Lord Rhondda that old age was a transferable disease, and for his avoidance, as far as possible, of the society of the aged on account of the risk of contagion. Association with the young keeps one more or less of the same age, very probably by suggestion to the unconscious, or in Oliver Wendell Holmes's words "While we've youth in our hearts we can never grow old." From experience at the Royal Hospital, Chelsea, where there are 500 pensioners, Thompson and Todd[3] are convinced of the powerful factor of lowered mentality due to loss of self-reliance, self-respect, and the instinct of self-preservation in inducing premature

[1] Finot, J., *Rev. mondiale*, Paris, 1922, xxxiii. 387.

[2] *The Mirrors of Downing Street*, by a Gentleman with a Duster, p. 165, 1920.

[3] Thompson, R. J. C., and Todd, R. E., *Lancet*, 1922, i. 874.

senility, and have been most successful in counteracting this by antidotal suggestion conveyed by cheerful chaff and by the avoidance of sympathetic condolence.

In addition to the *joie de vivre* a happy disposition that thinketh no evil, has no jealous suspicions, and is free from the tendency to worry has an important influence in keeping the mind and body young. The power of detachment from work and anxieties, as if the mind were fitted with thought-tight compartments, is a valuable asset in maintaining vitality unimpaired ; this was a trait in Gladstone and Kitchener.

Professional men who retain their offices as in the Church, the Civil Government, the Bar, tend to live longer than business men who retire to leisured ease after a strenuous struggle. B. Yeo's [1] analysis of 42 Bishops and Deans, 49 Judges, and 188 Peers, showed that in all three classes the average duration of life was practically the same, namely, 72 years. Among churchmen mention may be made of Cardinal de Salis (110), Gregory IX. (100), Abbé Maignon (100), Martin Routh (100), for 63 years President of Magdalen College, Oxford, thus surpassing the more modern

[1] Yeo, B., *XIX. Century*, 1883, xxiii. 390.

instance of Edward Atkinson, aged 96 years, for 59 of which he was Master of Clare, but not that of Laurence Chaderton (1536–1640) who, after being Master of Christ's College, Cambridge, with great success for 38 years, survived for 18 years and became a centenarian. There are some remarkable examples of artists retaining an active life to a very advanced age, such as Titian, Giovanni Bellini, Michael Angelo, Sidney Cooper. Politics often keep men busy and active to an advanced age, and the names of Palmerston, Brougham, Lyndhurst, the octogenarian premiers Gladstone and Clemenceau, Strathcona, Sir Charles Tupper naturally come to one's mind. In the legal profession Chief Justices and Judges can retain their seats and so keep up their vigour long past what is regarded in some walks of life as the retiring age. Sir Edward Coke (82), Lord Mansfield (89), Lord Brampton (90), Lord St. Leonards (93), and Lord Halsbury (97), are examples in point. Within recent years there have been two octogenarian Lord Mayors of London, Sir Thomas Crosby (in 1911), and Sir John James Baddeley (1921); the first created a record by being the first medical man to hold this office, and Sir John Baddeley celebrated his year of

Mayoralty by bringing out a beautiful historical account of Cripplegate.

From the inevitable exposure to infection and worry the medical fraternity is generally considered to rank low in the professions as regards longevity, but it is easy to point to exceptions especially among those whose mental vigour made them prominent in their own and in one instance for all time. Hippocrates is variously stated to have died at the ages of 85, 90, 104, or 106 years with the words "I leave behind me two great physicians, temperance and frugality." [1] I have references to 43 medical centenarians for 18 of which, including the record of W. G. Meade, physician at Tunbridge Wells and buried at Ware, Herts, in November 1652, aged 148¾ years, I am indebted to my friend Mr. R. R. James. The only one that I knew personally was Sir Henry Pitman, for 31 years (1858–89) and until his 82nd year Registrar of the Royal College of Physicians of London. Among the others Dr. de Bossy of Paris may be mentioned as the son of a centenarian. From analysis of 2113 eminent medical men Drinkwater [2]

[1] *Vide* F. Adams, *Genuine Works of Hippocrates*, Sydenham Society, vol. i. p. 10, 1849.

[2] Drinkwater, H., *Practitioner*, London, 1914, xciii. 844.

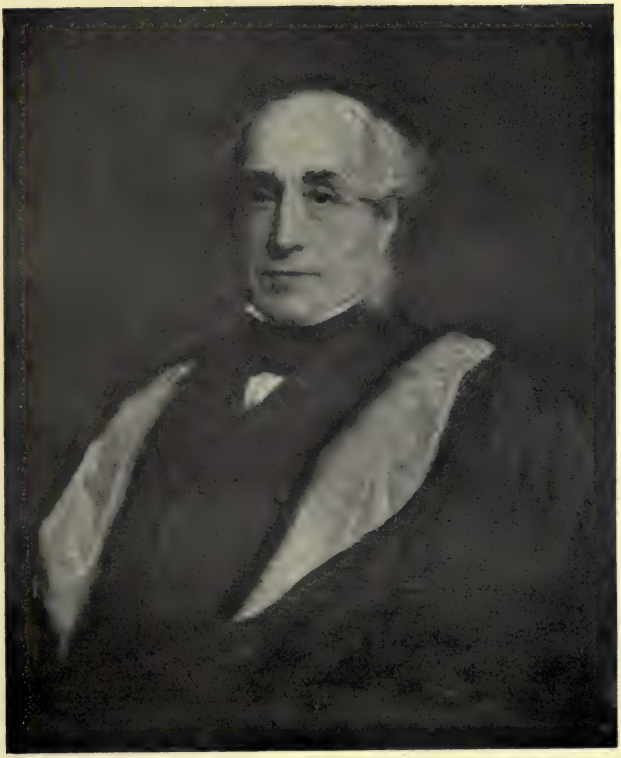


FIG. 9.—Sir Henry Alfred Pitman (1808–1908), M.D., Camb., F.R.C.P., Registrar of the Royal College of Physicians of London, 1858–1889.

From portrait in the Royal College of Physicians of London, painted in 1886 by W. W. Ouless, R.A.

found that the average age was 67 years, or considerably above the average age of the male population over 21 years, which was estimated at 59 years, and that 627 or nearly a third of them all were between 71 and 80 years of age.

But the examples given of mental activity late in life, and they could easily be multiplied,[1] are exceptions to the rule that the majority of men begin to fail in their work between 60 and 70. This no doubt is because most septuagenarians suffer in greater or less degree from pathological old age. In the case of the healthy vigorous man enforced retirement at the age of 65 or 70 is not to the advantage of either the retiring victim or the community, for it restricts his opportunities for production and useful activities guided by ripe experience. To quote examples of epoch-making work done by men long past the age when the majority have lost originality, initiative, and elasticity of mind: Galileo, Newton, Charles Darwin, Sophocles, Voltaire, Molière, Goethe, Michael Angelo, and Titian, made original and lasting contributions to science, literature, and

[1] For a consideration of this subject see Sir Hermann Weber's *Means for the Prolongation of Life*, and Dr. Lapthorn Smith's book *How to be Useful and Happy from 60 to 90*, London, 1922.

art long after fifty. Morgagni's famous *De Sedibus et Causis Morborum*, brought out when he was 80, and the Commentaries of W. Heberden (aged 91), published posthumously, represent the accumulation of many years and so cannot be fairly quoted as examples of ability persisting into late life. Rules and regulations must, however, be based on what is best for the majority and hence, though the exceptions are prominent and regrettable, the age limit of 65 to 70 must at present be accepted as generally advisable for otherwise permanent appointments.

Although functional activity maintains the tissues in a state of health, it is not an infallible panacea for the prolongation of life ; in the first place the danger of overwork and excessive fatigue must be borne in mind. While the attractive suggestion that excessive functional activity leading to extreme hypertrophy may exhaust the vitality of the tissues and lead to atrophy, may not be borne out by the examples quoted in its favour, such as the occupational neuroses and atrophy of the upper arm muscles in hammermen and file-cutters, there is some reason to retain a belief that this sequence of events may occur, for example in dilatation of the extremely hypertrophied hearts seen in

long-continued high blood pressure, renal disease, and valvular lesions;[1] but even here the possibility of other degenerative changes, due to toxaemia, must be borne in mind. Further, functional activity while keeping the cells of the body in a healthy state depends on their structural integrity, and this in its turn is the outcome of the modifications due to environment, and possibly of the inborn lease of vitality. So that although an active life may within limits prolong life, there are many instances in which, from extrinsic pathological influences or inherent inadequacy, it fails to do so, and a man becomes unequal to the demands of his position.

Personal Habits

All experience, medical and lay, such as is embodied in Cornaro's oft-quoted memoirs, Leonardus Lessius's *Hygiasticon or the right course of preserving life and health until extreme old age* (1613), George Cheyne's *Essay of Health and Long Life* (1724), Metchnikoff's orthobiosis, and the Arabian proverb of the ninth century, quoted by Lacassagne,[2]

[1] Compare Allbutt, C., *St. George's Hosp. Rep.*, 1870, v. 43, and C. Hilton Fagge, *Principles and Practice of Medicine*, 1886, vol. ii. p. 22, London.

[2] Lacassagne, A., *L'Homme vers la fin de sa vie*, p. 44, Lyon, 1919.

that "the greatest dangers for an old man are a good cook and a young wife," is in agreement as to the immense importance of strict moderation in indulging the appetites for the prolongation of life. The life histories of centenarians show that they have usually been small eaters, especially of meat. This is generally explained in terms of minimizing toxaemia, and it has been said that "man does not die, he kills himself" (Montaigne) and more graphically, if coarsely, that "he digs his grave with his teeth." In some lower forms of life, such as the planarians (Child), partial starvation and the resulting reduction lead to rejuvenescence and so to the inhibition of the onset of senescence; hibernation has somewhat the same effect, though perhaps this might be partly explained as merely starvation during prolonged sleep. The question has often been raised whether partial starvation in man has any such positive influence, and unprofessional "cures" on these economical lines have not been unfashionable. It might indeed be argued that the Allen treatment of diabetes, in which starvation is followed by increased carbohydrate tolerance, depends on a certain degree of rejuvenescence. Cures consisting in purgation may act by

partial starvation as well as by obviating toxaemia. After a period of starvation a normal person may become heavier than before, and his general health be improved. But in the present state of our knowledge and in the light of the dangers of starvation the further investigation in man of this problem is one that demands serious hesitation.

As to the bad influence of alcohol on longevity there can be no reasonable doubt. Alcohol is a protoplasmic poison causing degenerative changes in the cells and reducing the resistance to infection. A collective investigation undertaken by Sir Isambard Owen [1] showed that there were very few hard drinkers among the long-lived, and Sir George Humphry concluded that the characteristics of the aged included temperance ; among 46 centenarians one, and among 73 men over 90 one confessed to taking too much occasionally, and out of 298 men between 80 and 90 years of age 45, or 15 per cent, were classified as taking much alcohol. That such exceptions occur is explicable by great inherent vitality. It has been said that " wine is the milk of old people," but from his experience of the hygiene of the elderly Sir Hermann Weber was not in

[1] Owen, I., *Brit. Med. Journ.*, 1888, i. 1312.

sympathy with this view, and he pointed out the weakness of the popular idea that the moderate enjoyment of alcohol was harmless ; for so-called moderate drinking is in reality often immoderate indulgence for the individual, and most of us must have recognized from observation that long-continued though moderate use of alcohol is followed by premature deterioration. The proverb *vinum lac veneris* and the tendency that alcohol has to lead to incontinence and so to venereal infection may be borne in mind in considering its influence on longevity. As a medicine alcohol has its occasional use, and though it may be a food it is an expensive one.

Smoking among centenarians was specially investigated by Sir George Humphry, who found that among 19 male centenarians 8 smoked much, one a little, and 10 not at all ; while out of 30 female centenarians 4 smoked much, 2 moderately or little, and 24 not at all. There is no doubt that with advancing years there is commonly a relative loss of tolerance for tobacco, so that unpleasant symptoms ranging from cardiac extra-systoles, through abdominal pain, to tobacco angina, may dictate discontinuance of the habit. But a large number of old people have smoked in earlier life though subsequently non-smokers.

Personal tolerance to tobacco shows great variations, and there is no doubt that well-marked symptoms may be caused by tobacco. But that moderate smoking diminishes the chance of longevity has certainly not been proved. Much discussion has taken place as to the relation between smoking and arterio-sclerosis ; it is true that in animals nicotine in considerably larger doses than can be absorbed by smokers, damages the arteries, and Huchard and Lazarus were convinced that it caused arteriosclerosis. Sir Clifford Allbutt,[1] after quoting the various opinions, points out that if tobacco be a cause of arterial disease, it acts very slowly, for at 45 years of age, after a quarter of a century's exposure, the smoker's arteries are not distinguishable from those of the abstainer's ; and he mentions the arteriosclerosis of the ancient Egyptians and of women as incidents detracting from any argument that tobacco is an important cause of arterial disease.

A large proportion of the centenarians and persons over 80 years of age collected by Sir George Humphry obeyed the adage early to rise and early to bed, and I well remember

[1] Allbutt, C., *Diseases of Arteries, including Angina Pectoris*, vol. i. p. 250, 1915, London.

that he used to lay stress on the factor of getting up directly one woke and so denying the flesh the luxury of further sleep. Whether going to bed early and getting up early is more than an index of a life otherwise spent in accordance with the late Sir Andrew Clark's "laws of physiological righteousness" may be questioned.

Bodily Conformation.—Long-lived people are usually spare, obesity being rare, and, allowing for some shortening due to age, of a good average height (Humphry). It is interesting in this connexion to quote the conclusions arrived at by Robertson and Ray [1] from comparison of groups of long-lived and short-lived white mice in similar conditions. The long-lived were relatively stable, highly resistant to external disturbing factors, displaying subnormal variability and a more or less well-marked, but not invariable, tendency to early overgrowth and relative paucity of tissue accretion in late life; while the short-lived animals showed exactly the opposite features with a tendency to rapid increase of tissue in late life.

The importance of a healthy life with plenty of fresh air, sunshine, exercise, proper

[1] Robertson, T. B., and Ray, L. A., *Journ. Biol. Chem.*, 1920, xlii. 71.

diet, and absence of worry hardly needs insistence. Leonard Williams [1] has epigrammatically summed up the hygiene of old age as "Fresh air, meagre fare, freedom from care."

[1] Williams, L., *Minor Ailments*, p. 319, 1920, London.

V

THE CAUSES OF SENESCENCE AND GENERAL ATROPHY: LIMITED VITALITY OF CELLS—INFLUENCE OF THE ENDOCRINE GLANDS—METCHNIKOFF'S PATHOLOGICAL EXPLANATION

SENESCENCE AND CARCINOMA

The causation of old age is so complex that it is not possible to argue with any conviction that any one of the following explanations exclusively solves the problem satisfactorily.

Limited Vitality of the Cells

To explain the atrophic processes normal to old age it has naturally been assumed that the constituent cells are endowed with a certain store of vitality for themselves and their descendants, and that as this becomes exhausted the process of involution begins. This conception of an inherent limit of life is probable from the analogy of the existing limit of height and size, though in certain plants and trees

growth in size and length of days do not show a natural limitation. The process of ageing of the cells is thus regarded as just as much part of their development or life cycle as are their earlier and progressive stages. The exception is that the reproductive cell when it meets with its complement—the ovum with the spermatozoon—and as it were with new blood, starts a fresh lease of life, and so in Sir Edward Sharpey-Schafer's [1] words "we can only be immortal through our descendants." That there is a more or less definite cycle during which the cells multiply and after which they cease to do so receives support from the anatomical and physiological changes in old age ; thus the ovary undergoes fibrotic atrophy and ceases to be actively functional after the menopause. The atrophy or hypoplasia of the organs is due to diminution of the proliferation of the constituent cells. This is well shown in the lymphatic glands and spleen which are so active in youth and atrophied in advanced life. Salimbeni and Gery [2] point out that the hypoplasia in the woman aged 93 whom they minutely examined was most

[1] Sharpey-Schafer, E. A., Presidential Address, Brit. Assoc., 1912, *Brit. Med. Journ.*, 1912, ii. 589.

[2] Salimbeni et Gery, *Ann. Inst. Pasteur*, Paris, 1912, xxvi. 577.

prominent in the lymphatic tissues and the bone marrow which have to supply the cells most constantly needed. Even in the lowest forms of life senescence and death would occur in the absence of the rejuvenescence associated with reproduction. In the complex congeries of cells making up the higher animals and man this rejuvenescence does not accompany reproduction, and the vitality of the constituent cells diminishes until eventually atrophy and death supervene.

Many of the vital phenomena of cells may, as Martin Fischer,[1] Lumière,[2] and others point out, be interpreted in terms of the behaviour of simple hydrophilic colloids. Bechhold[3] has shown that, like a simple colloidal jelly, the cells of the human body, which are colloidal masses, lose their affinity for water progressively with age and become less elastic ; the water content of the fetus being 94 per cent, as compared with 70 per cent at birth and 58 per cent in adult life, thus recalling the old idea of the dryness of elderly bodies. According to Marinesco[4] dehydration of the colloids

[1] Fischer, M. H., *Oedema and Nephritis*, 1921, New York.

[2] Lumière, A., *Rôle des colloïdes chez les êtres vivants*, 1921, Paris.

[3] Bechhold, H., *Die Kolloide in Biologie und Medizin*, Dresden, 1912.

[4] Marinesco, G., *Études histologiques sur le mécanisme de la sénilité*, 1904 ; also *Presse méd.*, Paris, 1922, xxx. 309.

in the cells is an inherent progressive change in evolution and leads to senescence and death. It has also been thought that as the result of differentiation and metabolism the cell protoplasm may become overladen with products inimical to its vitality, which it cannot, as can the protozoa, utilize for rejuvenation, and which hinder metabolism. The micellae, or aggregations of albumin constituting the colloids of the cells, alter in structure and become more stable until the colloid state disappears and the cell accordingly dies (Lumière, Danysz). Such changes must obviously be greatly influenced, as H. Campbell [1] and others have insisted, by their environment ; the individual cells are in some degree of material continuity by " protoplasmic bridges " which probably serve not only for nutritional purposes but also for the transmission of physiological impulses. It also appears that the life cycle of the cell is determined not so much by time as by the interaction of the tissues and the plasma. By cultivating connective tissue in the plasma of chickens of different ages Carrel [2] showed that its growth was more abundant in the plasma of younger

[1] Campbell, H., *Treatment*, London, p. 153, 1909.
[2] Carrel, A., *Journ. Exper. Med.*, Baltimore, 1913, xviii. 287.

chickens than in that of older ones. Working on these lines Loeb and Northrop [1] concluded that the duration of life was determined either by a substance leading to old age or by the destruction of a substance which normally prevents old age and natural death. More recently Carrel and Ebeling [2] found that in these cultures of connective tissue the rate of multiplication of fibroblasts and the duration of life *in vitro* varied in inverse ratio to the age of the animal from which the plasma was taken, and that this depended on the presence of an inhibitory body in the plasma of older animals. These experiments recall the practice centuries old of transfusion of young persons' blood into the old which, however, led to disastrous results on account of a technique now known to be dangerous. Whether with modern methods success will be obtained remains to be proved, but probably repeated transfusions would be required. But to return to the subject : Carrel, Champy, and Grandcourt have shown that, with frequent washings to remove waste products, tissue cells can be cultivated indefinitely for years *in vitro*, and in

[1] Loeb and Northrop, *Journ. Biol. Chem.*, 1917, xxxii. 103.

[2] Carrel, A., and Ebeling, A. H., *Journ. Exper. Med.*, Baltimore, 1921, xxxiv. 599.

themselves have an unlimited capacity for multiplication ; it therefore appears that the ageing of cells in the living organism is determined by extrinsic factors in the plasma rather than by any inherent limitation in the cells. In the ordinary conditions of life senescence of the cells might be regarded as the result of increasing differentiation and, possibly from accumulation of material which cannot be utilized for rejuvenation, of diminished metabolic activity. In the physiological life of gland cells, for example, the salivary glands and pancreas, granules are manufactured and discharged, but the hypothetical material which collects in elderly cells, of which pigment may possibly be an example or the visible sign, remains in these cells and hampers their functional activity. As atrophy of the functional cells and increase of connective tissue are regarded as characteristic of senescence, and a high proportion of cells as characteristic of embryonic life, Robertson and Ray [1] suggest that the potential longevity of any individual is determined by the relative velocities of anabolism in the cells on the one hand, and in the fibrous tissue on the other hand. A low rate of cellular anabolism increases the growth of the cells and delays the

[1] Robertson, T. B., and Ray, L. A., *Journ. Biol. Chem.*, 1920, xlii. 71.

increase of fibrous tissue ; this they were able to effect by feeding white mice with tethelin. The relations of the functionally active cells and the connective tissues have also been investigated by Nathan [1] and his collaborators, who bring forward experimental evidence in favour of the modified view that while dense connective tissue inhibits cellular proliferation, young loose connective tissue favours the multiplication of cells in proportion as it approaches the structure of the embryonic mesenchyma. Drew's [2] observations on the culture of tissues and tumours show that the stroma acts like embryonic tissue in favouring growth.

To sum up : the cells of the complex organism depend for their duration of life not so much on an inborn store of vitality as on metabolic changes in the colloids which in their turn are modified or controlled by extrinsic factors of various kinds.

Relation of the Endocrine Glands to Senescence

As the metabolic activities of the cells of the body generally are markedly influenced

[1] Nathan, *Ann. de méd.*, Paris, 1922, xi. 59.
[2] Drew, *Brit. Journ. Exper. Path.*, London, 1922, iii. 20.

by the secretions of the ductless glands, the relations between these endocrine glands and senescence demand some discussion.

The process of reproduction leads to rejuvenescence in the protozoa, and it might therefore be imagined that in the higher animals continued activity of the sexual glands would similarly exert a rejuvenating influence on the remaining cells of the body. But the process of specialization has gone so far in the cells of the higher animals that the highly differentiated cells, especially of the nervous system, cannot fairly be compared with the constituent molecules of a unicellular organism. As sexual activity is the biological reason for existence and as in vigorous men sexual power may last long beyond the usual period, man being regarded as old as his sexual glands, it has been widely imagined that the functional activity of the sex glands is in some way a cause, rather than a manifestation, of the preservation of bodily vigour, and conversely that failure and atrophy of the sexual glands cause old age and senility. There is an attraction, though not without the danger of fallacies, in interpreting the words of older writers as prophetic anticipations of quite modern knowledge. But with this caution in

mind there is some ground for crediting Hufeland [1] with some idea of the internal secretion of the sexual glands : as long ago as the end of the eighteenth century he wrote " the organs of generation have the power of secreting the finest and most spiritual parts of our nourishment ; but at the same time they are so organised that these perfected and ennobled juices can again return and be received into the blood. Like the brain, therefore, they belong to those important organs which serve for bringing to perfection and ennobling our organic matter and power, and even ourselves."

Since 1889 when Brown-Séquard, at the age of 72 (6 years before his death) put forward the idea that rejuvenation could be brought about by the hypodermic injection of testicular emulsion, the view that old age and senile changes are due to failure of the glands of internal secretion has become popular. The thyroid (V. Horsley, Léopold-Lévi), the testis and ovary, or most or all of the glands (pluriglandular insufficiency) have been incriminated ; Lorand,[2] indeed, regards old age as a disease caused by degeneration of not one but several

[1] Hufeland, C. W., *The Art of Prolonging Life*, 1797, vol. i. p. 227.
[2] Lorand, A., *Old Age Deferred*, pp. 51, 114, Philadelphia, 1921.

of the endocrine glands, Biedl[1] expresses much the same view in referring old age to a disturbance of the endocrine balance, and Berman[2] in a recent semi-popular book states that old age is an exhaustion permanent and irreparable of all the glands of internal secretion ; like Lorand he ascribes considerable importance to failure of the internal secretions of the sexual glands. It is highly desirable to arrive at some conclusion as to the relation between changes in the glands of internal secretion and senescence, for in medical practice this conception of cause and effect has been acted upon ; various glandular extracts have been employed to counteract and delay the disabilities that may accompany advancing years and, though not so freely, operations, viz., ligature of the vas deferens and implantation of testicular grafts, have been carried out.

Lydston[3] implanted testes from boys recently dead into men with atrophied or destroyed testes and reported improvement. Stanley and Kelker[4] implanted 11 cases

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[1] Biedl, A., *Endocrinology*, Los Angeles, 1921, v. 523.

[2] Berman, L., *The Glands Regulating Personality*, p. 260, The Macmillan Co., 1921, New York.

[3] Lydston, G. F., *Journ. Amer. Med. Assoc.*, Chicago, 1919, lxxii. 396.

[4] Stanley and Kelker, *Journ. Amer. Med. Assoc.*, Chicago, 1920, lxxiv. 1501.

with testicular grafts obtained from executed criminals, and 5 cases with the testes of rams, obtaining improved general condition, though not claiming that life was prolonged. Stanley [1] injected by means of a large syringe strips of testes of rams, goats, or bears under the skin of the abdomen of more than 300 prisoners, and stated that conditions of neurasthenia and senility were relieved.

The stimulating effect of thyroid secretion on growth and metabolism, shown both experimentally and clinically in the therapeutic triumphs of thyroid treatment in myxoedema and hypothyroidism, seems to justify the view that failure of thyroid function plays an important part in reducing the capacity for multiplication and regeneration of cells. Between the manifestations of hypothyroidism and those of old age there are undoubtedly striking resemblances, such as the dry skin, the loss of hair, the diminished mental and bodily energy, and the increased amount of interstitial fibrous tissue. In some respects myxoedema and cretinism imitate the senile state ; myxoedema has indeed been described as more than a simulation and as the best example of secondary senilism (Hastings Gilford [2]) ; but this is a very different condition from healthy old age

[1] Stanley, *Endocrinology*, Los Angeles, 1921, v. 708.

[2] Gilford, H., *The Disorders of Post-natal Growth and Development*, p. 643, 1911, London.

which does not present the picture of complete loss of thyroid function ; old age therefore cannot be regarded as due to athyroidism. Usually atrophy of the thyroid accompanies and corresponds to that of the senescent body as a whole. No doubt pathological changes may occur in the thyroid, especially in women, during advancing years, and it is in such instances that thyroid feeding produces so much improvement that it has revived in our day the hope of an elixir of life and perpetual youth. It is not improbable that the administration of thyroid gland extract may, by preventing high blood pressure, delay or obviate the onset of arteriosclerosis, and so stave off senility due to this cause, but this is pathological old age and not the physiological involution.

In addition to the seminal tubules and ova, which provide their external secretion, the testes and ovaries contain the interstitial cells described by Bouin and Ancel [1] or, in Steinach's phrase, " the puberty gland " ; the germ cells and the interstitial cells differ from each other in structure, function, and reaction to external influences ; thus the germ cells though

[1] Bouin et Ancel, *Compt. rend. Acad. Sc.*, Paris, 1903, cxxxvii. 1289, 1904, cxxxviii. 110.

dominant are more susceptible to damage, for example by ligature of the vas deferens, *x*-rays, alcoholism, or pressure, as in the case of a cryptorchid. It is stated that when the seminal tubules are active and prominent the interstitial cells are scanty, and conversely that when the seminal tubules atrophy the interstitial cells multiply; Lipschülz, Ottow, Wagner, and Bormann[1] showed that hypertrophy of the interstitial cells as observed in various experimental conditions depends on local factors in the testes and has nothing to do with their internal secretion in relation to the body as a whole. After ligature of the vas deferens in animals there are, according to Steinach, Kuntz,[2] and others, two stages (1) the seminal tubules atrophy while the interstitial cells multiply, and (2) after some time the seminal tubules regenerate while a certain amount of increase in the interstitial cells persists. Nathan[3] ascribes the regeneration of the seminal tubes to the influence of the interstitial cells, which he considers act like young connective tissue by favouring growth. The interstitial cells of Leydig in the testis and the interstitial or

[1] Lipschülz, Ottow, Wagner, and Bormann, *Proc. Roy. Soc.* Lond., 1922, ser. B, xciii. 132.

[2] Kuntz, A., *Endocrinology*, Los Angeles, 1921, v. 190.

[3] Nathan, *Presse méd.*, Paris, 1922, xxx. 237.

lutein cells of the ovary are generally regarded as responsible by their lipoid internal secretion or hormone for the secondary sex characteristics (Bouin and Ancel, K. Sand [1]), though Blair Bell [2] and Sternberg [3] deny this. Sir Frederick Mott,[4] who has extensively investigated the interstitial cells, especially in connexion with dementia praecox and other forms of mental degeneration, concludes that in fetal life they act as sex determinants, and that later in life they are responsible for the sexual appetite. It has been argued that atrophy of the interstitial cells is the cause of senescence. Against this view is Sir Frederick Mott's observation that after birth the interstitial cells undergo progressive atrophy and disappear, that they reappear and are in a state of functional activity at puberty (a sequence of events described by Aron [5] as two different interstitial glands), and that they are present in extreme old age ; Retterer [6] also described their presence in the testes of men over 70 years of age. So far it might be concluded

[1] Sand, K., *Journ. de physiol. et de path. gén.*, Paris, 1921, xix. 525.

[2] Blair Bell, *The Sex Complex*, p. 28, 1920.

[3] Sternberg, *Berl. klin. Wchnschr.*, 1921, lviii. 556.

[4] Mott, F. W., *Brit. Med. Journ.*, 1919, ii. 658 ; *Proc. Roy. Soc. Med.*, 1922, xv. (Sect. Psychiat.), 1-30.

[5] Aron, *Compt. rend. Soc. biol.*, Paris, 1921, lxxxv. 107.

[6] Retterer, E., *Compt. rend. Soc. biol.*, Paris, 1919, lxxxii. 423.

that changes in old age, such as diminution in number and pigmentation, shown by the interstitial cells, are not the cause but an accompaniment of senescence.

Kenneth Walker's [1] observation that the interstitial cells of the testis show a gradual diminution in number from the age of about 30 years, might be quoted in favour of the contention that atrophy of these cells plays a part in the production of senescence. In addition there are the dramatic experiments on rats carried out by Eugen Steinach,[2] who was formerly Professor of Physiology in the German University of Prague and since 1912 has been Director of the Physiological Section of the Experimental Biological Institute at Vienna. He found that in apathetic senile rats with degenerative changes in the thyroid, pituitary, and interstitial cells ligature or section of one vas deferens causes atrophy of the seminal tubes and active growth of the interstitial cells ; the hormone thus provided stimulates the thyroid, pituitary, and brain, and the rat is rejuvenated, the sexual instincts and emotions become active, and the rat may

[1] Walker, K., *Brit. Med. Journ.*, 1922, i. 297.

[2] Steinach, E., *Verjüngung durch experimentelle Neubelebung der alternden Puberstätsdrüsen*, J. Springer, Berlin, 1920.

have offspring ; when relapse into senility occurs, a repetition of the operation on the other side brings about a further rejuvenation ; and later the same result is effected by grafting the testes of a young rat. In this way life is definitely prolonged. This procedure has been advocated in man with some success by Steinach ; Lichtenstern of Vienna, who has done 36 such operations and 21 implantations on account of senile changes, has not encountered any bad results, but admits that he has not been uniformly successful, and that the number of cases is not sufficient to justify a final conclusion. From observation in Vienna Benjamin[1] estimated that the operation was followed by no results at all in from 10 to 20 per cent of the cases. Obviously a considerable time must elapse before any decision as to prolongation of life can thus be assured.

In the autumn of 1921 a man aged 70 was advertised to speak at the Albert Hall on " How I was made 20 years younger by the Method of Dr. Steinach of Vienna," but he died on the morning of the day from pneumonia (Benjamin[1]), the necropsy not revealing, so it is said, any trace of an operation ; the hypertrophy of the interstitial cells, however, may have been induced by the exposure of the testes to *x*-rays.

[1] Benjamin, H., *New York Med. Journ.*, 1921, cxiv. 687.

Steinach's observations naturally aroused great interest and have been repeated with discordant results by a number of investigators : Simmonds [1] and Tiedje [2] have failed to confirm the occurrence of the changes in the testes after vasectomy ; and Romeis [3] and Marinesco [4] have not obtained the striking clinical results described by Steinach. Levy Lenz and Schmidt,[5] however, report rejuvenation in 23 out of 24 cases of vasectomy, and Voronoff encouraging results from implantation of chimpanzee's testes into man. But Marinesco compares Steinach's published results with those of Brown-Séquard.

It may be added that the operation of ligature of the vas deferens which was performed some 25 years ago, before prostatectomy became established, in order to cause atrophy of enlarged prostate, was not noticed to be followed by rejuvenescence. Mr. C. Mansell-Moullin, who published [6] a series of 14 such cases, has kindly informed me that his patients did not

[1] Simmonds (quoted by Marinesco), *Deutsche path. Ges.*, Jena, 1921.

[2] Tiedje, H., *Deutsche med. Wchnschr.*, 1921, xlvii. 35.

[3] Romeis, B., *München. med. Wchnschr.*, 1920, lxvii. 600, 1821.

[4] Marinesco, *Presse méd.*, Paris, 1922, xxx. 309.

[5] Lenz, L., und Schmidt, P., *Deutsche med. Wchnschr.*, 1921, xlvii. 327.

[6] Moullin, C. W. M., *Enlargement of the Prostate*, p. 194, 3rd edition, 1904.

show any evidence of such a change. Romeis has also raised this objection to Steinach's results which it has been thought might be explained by suggestion (Freudenberg)—a view hardly tenable in the light of the remarkable results described in animal experiments.

The internal secretion of the ovary has never been isolated, and the evidence of its existence rests on the results of removal. Castration in men and in women does not bring on the phenomena of old age, though this operation is followed by well-marked changes as regards the secondary sex-characters, and, according to Voronoff, eunuchs are short-lived. It may also be pointed out that the obesity so common after castration is not a feature of " the lean and slippered pantaloon." Further, after the menopause the ovaries undergo fibrotic atrophy, and it appears from Professor Turnbull's observations (*vide* p. 114) that the interstitial cells are very scanty or absent ; further observations are necessary as to the presence of interstitial cells in senescent ovaries, but presuming that they are scanty it would follow, on the hypothesis that the interstitial cells exert an influence in preventing the onset of old age, that women should become old much sooner than men in whom the interstitial cells are apparently much

more in evidence. It cannot of course be admitted that such a difference in the sex incidence of old age exists. The improved health and rejuvenation after *x*-ray treatment for metrorrhagia and uterine fibromyomas at the climacteric or post-climacteric age have been regarded by Steinach and Bordier as due to hypertrophy of the ovarian interstitial cells following induced atrophy of the ova, but to accept this there must be definite evidence that the interstitial cells are increased in number. Harrower's [1] dictum that the absence of a hormone provided by the interstitial cells is responsible for premature senility does not appear to be borne out by our present knowledge, but a great deal of further work must be done before a final decision is justified.

Testicular and ovarian extracts, often in combination with those of the thyroid and pituitary, which are known to have a definite physiological action, have been extensively used as a panacea. But is there any undeniable evidence that the extracts of testis and ovary so far employed have any effect apart from that of suggestion? According to Frank [2] the available ovarian preparations are defatted and thus

[1] Harrower, *Practical Hormone Therapy*, p. 344, 1914.
[2] Frank, *Journ. Amer. Med. Assoc.*, Chicago, 1922, lxxviii. 181.

deficient in the potent lipoid extracts ; and very serious doubts as to the activity of testicular extracts have been expressed by Professor Cushny.

The possibility must be borne in mind that the use of thyroid and other gland extracts that have a definite effect on metabolism is not devoid of risk to cells that are gradually undergoing involution; for, by stimulating metabolism unduly, the existing vitality may be prematurely exhausted and, though for a time there is a gratifying show of energy, it is but a flash in the pan that precedes a more rapid loss of function. We are irresistibly reminded that " no man putteth new wine into old bottles : else the new wine doth burst the bottles."

At the present time it would be unwise to express a dogmatic opinion about the relation of the endocrine glands to normal old age. That old age is due to endocrine insufficiency or loss of balance cannot be regarded as proved, and it is probably safer to regard changes, such as atrophy, in the various glands of internal secretion as concomitant with, rather than causal of, those in the senescent body.

Metchnikoff's Pathological Explanation

As an alternative to the belief that there is an inherent quantum of vitality which may be harmfully or beneficially influenced by environment and the wear and tear of life, it has been suggested that the process of ageing depends solely on external factors and that either there is no intrinsic limitation to the life of the organism or that the possibility is entirely cast into the shade by predominance of extrinsic influences. This doctrine is free from any tinge of fatalism and has the advantage that it is a direct stimulus to efforts in the direction of hygiene in all its forms ; for as things are now old age owes its discomforts to superadded and in most instances avoidable complications. Élie Metchnikoff, as is well known, attributed the senile accompaniments of advanced years to pathological and preventible causes, namely toxaemia induced by alcohol, syphilis, and especially by bacterial activity in the colon which in common with Barclay-Smith and Arbuthnot Lane, he regarded as a harmful phylogenetic relic, this point of view being expressed by the epigram " the longer the colon the shorter is life." He considered that the putrefactive bacteria in the colon produce phenol, indol,

skatol, and aromatic bodies which cause degenerative changes in the cells of the body ; and that the more resistant macrophages, which do not attack healthy tissues, absorb the damaged cells. He therefore employed means to prevent excessive bacterial activity in the large intestine, and in addition to care in diet so as to diminish the risk of introducing bacteria into the alimentary canal, he advocated the destruction of putrefactive bacteria in the colon by means of sour milk and cultures of *Bacillus bulgaricus*, which form lactic acid and thus render the contents of the bowel acid and unsuitable for the growth of the harmful micro-organisms. Metchnikoff thoroughly practised his doctrine, but he did not begin his regime until he was well over fifty, and, in spite of several severe illnesses which had damaged his heart, he lived longer than any of his family and passed the 70th milestone. His views on the method of production of senility aroused great interest and criticism not only from Marinesco,[1] Léri,[2] Sand, Laignel-Lavestine, and Voisin, who disputed the reality of the macrophages devouring the cells of the central nervous system, and Ribbert [3] who denied the existence

[1] Marinesco, *Études histologiques sur le mécanisme de la sénilité*, 1904.

[2] Léri, *Le cerveau sénile*, 1906.

[3] Ribbert, H., *Der Tod aus Altersschwäche*, Bonn, 1908.

of such a physiological intoxication and ascribed old age and death to the inevitable physico-chemical changes incident to life, but also from Salimbeni and Gery,[1] working in the Pasteur Institute, who while supporting most of his contentions did not consider that they provided the whole explanation, *e.g.*, the involution of the ovaries at a fixed age was not thus accounted for. The means Metchnikoff advised for the postponement of senility and death were on much broader lines than the popular conception summed up by "sour milk" might suggest, for he expounded the philosophy of orthobiosis or a correct method of living.

That intestinal toxaemia due to stasis has a very important influence in producing disease cannot be doubted, and Sir Arbuthnot Lane[2] has brought this prominently to our notice; while clothing in modern language the old ideas of the *primae viae* he recalls to our memory Abernethy's[3] panacea for many ills of the flesh, namely a blue pill at night followed by a mixture of gentian and senna in the morning.

[1] Salimbeni et Gery, *Ann. Inst. Pasteur*, Paris, 1912, xxvi. 577.

[2] Lane, W. A., *The Operative Treatment of Intestinal Stasis*, 1918, London.

[3] Abernethy, J., *The Constitutional Origin and Treatment of Local Diseases*, 1811.

Among his collaborators Mr. Ernest Clarke [1] has insisted on the premature ageing of persons with intestinal stasis. From the analogy of syphilis, alcoholism, and other intoxications, which may produce degenerative changes simulating those found in old age, the hypothesis of intestinal toxaemia gains a certain amount of support, and it may not be so easy to exclude the agency of intestinal toxaemia as in the case of syphilis and some intoxications. But intestinal toxaemia may, as far as can be judged, be absent in healthy old age, and conversely be present in early life without causing the phenomena of old age. Further objections have been raised :—why should intestinal toxins be harmless for 40 or 50 years and then exert such a serious influence ? why should women who are more subject than men to constipation be more long-lived ; and that in constipated persons the faeces, as shown by Schmidt and Strasburger, contain fewer living bacteria than in health.[2]

As applied to normal old age and death this hypothesis is pathological and therefore has rather failed to interest those who are working

[1] Clarke, E., in *The Operative Treatment of Intestinal Stasis*, p. 246, London.

[2] *Vide* Saundby, *Old Age, its Care and Treatment*, pp. 5, 28, London, 1913.

at the biological aspect. Perhaps the most that can be safely concluded in balancing the pathological and biological arguments is that while Metchnikoff's view may be partially true it does not account for all senile changes, and that normal old age or senescence cannot be regarded as the result of toxins absorbed from the alimentary canal.

Old Age of Cells and Carcinoma

The relation between ageing of the cells on the one hand and the development of carcinoma on the other hand is a subject of great interest. According to Karl Pearson's [1] statistical enquiry the incidence of carcinoma reaches its maximum at the age of 46 years in women and 56 years in men ; Lazarus-Barlow [2] concluded that the range of years over which cancer is likely to occur is practically the same in the two sexes, namely 46 to 64, and that among 4659 cases of malignant disease there were only 35, or 0·7 per cent, over 80 years of age.[3] The cancer age, therefore, coincides with the waning of maturity

[1] Pearson, K., *Arch. Middlesex Hosp.*, 1902, ii. 127.

[2] Lazarus-Barlow, W. S., *Ibid.*, 1905, v. 43.

[3] On analysis of the Registrar-General's returns for England and Wales (1901–1909) C. Singer (*Quart. Journ. Med.*, Oxford, 1911–12, v. 33), found that the incidence curves of carcinoma of the lip, face, and breast were exceptional in rising up to the highest age recorded (90).

and the onset of old age ; that carcinoma is rare in very old persons is also shown by the occurrence of one case only among 71 centenarians collected by Sir George Humphry. Laurent[1] considered that whereas longevity depends on a condition of vital equilibrium, the development of cancer is due to a want of this equilibrium, to a state of anarchy, and that the factors disposing to orderly vitality are conducive to longevity and antagonistic to the development of new growth. The reason why malignant growths are prone to appear with the onset of old age has naturally been the subject of much debate. According to Thiersch degeneration lessens the controlling influence normally exerted by connective tissue on epithelium, the inherent proliferative capacity of which then runs riot. Ribbert believed that from loss of resistance or diminution of surface tension in the connective tissues post-natal " rests " of epithelium were produced as the result of irritation and that these displaced cells then grew because there was no controlling opposition. Adami suggested a reversion of the highly specialized epithelial cells to a simpler form with powers of proliferation, the cumulative habit of growth taking the place

[1] Laurent, O., *Bull. Acad. de méd.*, Paris, 1919, lxxxi. 835.

of the habit of work, and practically anticipated the more modern view. According to Hastings Gilford [1] malignant disease is a premature cell senility and the result of the partial reversion of immature or adult cells to an embryonic or quasi-embryonic state. From a study of senescence in dogs Goodpasture [2] concludes that degenerative changes in the cells lead not only to death of some cells but to dedifferentiation of others, which, becoming simpler in structure and function, recover their juvenile power of growth in varying degrees, and that hence metaplasia and tumour growths occur as accidents of commencing old age. A little later Oertel [3] insisted on his view that cancer is not an embryonic reversion or a specific change in the cell but a phenomenon of senescence—a degenerative proliferation depending upon disturbances in the nucleus plasma relations, specifically upon the loss of nuclear chromosomes ; from age or degeneration the tumour cell loses the higher functional chromosomes and retains the genetically older and more resistant ones controlling reproduc-

[1] Gilford, H., *The Disorders of Post-natal Growth and Development*, 1911, London ; and *Brit. Med. Journ.*, 1913, ii. 1617.

[2] Goodpasture, E. W., *Journ. Med. Research*, Boston, 1918, xxxviii. 127.

[3] Oertel, H., *Ibid.*, 485.

tion and vegetative activities; thus there arises a race of cells without the differentiation of undegenerated cells.

These various expressions of opinion would justify the conclusion that with the onset of old age the degenerative processes in the cells lead to the production of less specialized cells which have the compensating property of more vigorous growth, and that in certain circumstances, one of which is very probably a diminished power of resistance on the part of the surrounding tissues and another, and very important one, irritation in some form or another, riotous proliferation of the cells invades the adjacent parts. That the conditions necessary are usually local is strongly suggested by the appearance of the new growth at one spot only and by the frequent absence of recurrence after free removal. There may be a premature local senescence of the tissues, just as there is premature old age of the body generally, and this would explain the exceptional occurrence of malignant disease in early life or long before the usual time.

VI

NORMAL STRUCTURAL CHANGES IN OLD AGE

Physiological old age, namely a process of involution and atrophy uncomplicated by superimposed pathological changes, is extremely rare ; pathological processes may initiate and hurry on a condition imitating old age, and indeed the morbid changes found after death in old people commonly show the lesions of past infections in addition to those of physiological involution, and the longer life lasts the greater the probability that changes due to disease will accumulate. It is therefore difficult to determine accurately where physiological involution ends and pathological lesions begin, and there has been much confusion between physiological old age and pathological senility. It must, on the other hand, be admitted that the ideal condition of physiological involution

without some definite evidence of superadded pathological change hardly ever comes before us. In fact at the best old age is almost always but relatively physiological, in other words, as Metchnikoff wrote in 1903, there is at present, from the conditions of inharmonious environment, no chance of a really physiological old age and death for mankind. But the view that old age is invariably the accumulated product of multiple injuries due to infection and poisons, or that it is due to arteriosclerosis (Boerhaave, Haller, Demange) is an entirely different proposition and does not fit in with biological knowledge. While fully recognizing the difficulties an attempt may be made to tabulate the natural changes accompanying and responsible for old age, and to contrast them with the pathological changes commonly complicating the normal structural involution of the human body.

The general atrophy of old age, as grossly shown by loss of weight, does not proceed equally in all parts of the body. The supporting fibrous tissues of the body and organs certainly atrophy less than the nobler, because actively functional, cells of the organs ; it is difficult to estimate the atrophy of the fibrous tissues, for from shrinkage of the parenchyma

of organs and of muscles the fibrous framework stands out in greater prominence. Some proliferation or replacement fibrosis follows atrophy of the nobler tissues, and pathologically infection may cause fibrosis. But that the fibrous tissue does to some extent share in the general atrophy is rendered probable on the analogy of the change in the allied tissue of bone which undergoes rarefaction and thinning. The subcutaneous and perivisceral stores of fat diminish out of proportion to the fibrous supporting tissues around them. The place of the fat in the fat cells may be taken by fluid —serous atrophy—or the cells may simply revert to the condition of connective tissue cells. In passing it may be pointed out that it is curious that with the diminished metabolism of old age the stores of fat are not increased as they are in similar circumstances in adult life ; Is it due to a widespread atrophy of the connective tissue cells that store fat ? If so, an accumulation of fat in the liver might be expected, but this is not so. Possibly it is the result of deficient assimilation. The heart, as Councilman[1] has shown, is on the whole better preserved than the other organs ; but

[1] Councilman, W. T., *Contributions to Medical and Biological Research*, dedicated to Sir William Osler, 1919, vol. ii. p. 918, New York.

it might well be argued that the existence of such a cardiac condition is a determining factor in the attainment of advanced age.

The skin is dry, thin, smooth, glossy from atrophy, inelastic like parchment, and is wrinkled from degeneration and disappearance of the elastic tissue, subcutaneous fat and muscular fibre. These changes are most advanced on the face, especially the forehead, and backs of the hands from exposure. The degeneration of the elastic fibres, recently studied by Kissmeyer and With,[1] gives a characteristic mesh-like appearance, depending on the rigid wrinkles, to the skin, which takes a yellow tint. The ivory pallor and coldness are due to the diminution in the capillaries ; the skin may show areas of pigmentation and leucodermia—changes described by Sir Lenthal Cheatle as due to the wear and tear of life (biotripsy) ; in a woman aged 93 Salimbeni and Gery described almost complete disappearance of the papillae and of the collagen fibres. The pigmentation has been regarded as a means of protection, for there is a relation between it and malignant disease, the latter being prone to occur when pigmentation fails

[1] Kissmeyer and With, *Brit. Journ. Dermat. and Syph.*, London, 1922, xxxiv. 175.

(Pringle[1]). These atrophic changes are far commoner on the backs than on the palms of the hands, and it is noteworthy that among Cheatle's[2] 200 collected cases of malignant disease of the hand there was one only on the palm. The subcutaneous fat is diminished in amount, which is regarded by Sir Arbuthnot Lane, though not with any special reference to old age, as one of the many results of colonic toxaemia. The yellow fat contains excess of cholesterol. There is diminished secretion by the sweat and sebaceous glands, and from this cause and the diminished vascularity there is less loss of heat to correspond with the slower metabolism.

Hair.—Greying or whitening of the hair occurs commonly in old age, but not universally for some centenarians have retained the natural colour of the hair ; coarse jet-black hair is specially prone to whiten early. The change in colour has been ascribed by Metchnikoff to the action of phagocytes (chromophages) which invade the roots of the hairs and carry off the pigment granules. Like the arcus senilis it may occur quite early in life

[1] Pringle, J. J., *System of Medicine* (Allbutt and Rolleston), 1911, ix. 549, London.

[2] Cheatle, G. L., *West London Med.-Chir. Journ.*, 1921, xxvi. 154.

and without any other indication of age, and is often hereditary ; as the sage of Norwich wrote, " Hairs make fallible Predictions, and many Temples early Gray have outlived the Psalmist's Period." [1] Lord Bacon [2] indeed said, " Hasty gray hairs, without baldness, is a token of long time ; contrarily, if they be accompanied by baldness." But baldness is often due to seborrhoea and so only secondarily connected with advanced age. In some rare instances the hair already grey or white has been known to regain its normal colour ; the late Sir Charles Cameron [3] recorded this event in his own life after an accident confining him to bed for some months in his eightieth year, and refers to the hair of a man aged 90 years returning to its original brown colour ; cases were also reported by Graves.[4] Velasquez de Tarente [5] recorded an abbess who after an illness which promised to be fatal in her hundredth year had a crop of brown hair, and, like Sir Charles Cameron, put on weight. Four other cases are given by Sir

[1] *Letter to a Friend*, in Greenhill's edition of *Religio Medici*, p. 135, Macmillan, 1898.

[2] Bacon, F., *The History of Life and Death.*

[3] *Autobiography of Sir Charles Cameron*, p. 137, 1920.

[4] Graves, R. J., *Dublin Quart. Journ. Med. Sc.*, 1847, N.S., iii. 339.

[5] Quoted by D. Roy, *Thèse de Paris*, No. 110, 1910.

John Sinclair [1] in persons aged 80, 104, 105, and 114 years. Baldness may be definitely due to thyroid insufficiency and not to atrophy of the hair follicles and sebaceous glands.

> A pensioner aged 75, whom I saw with Major R. J. C. Thompson, in the Royal Hospital, Chelsea, with baldness and a grey beard, was given thyroid extract, as he was thought to have hypothyroidism; his general condition then improved wonderfully, and his scalp became covered with dark brown hair which had to be cut at intervals. Parkinsonian tremor was rather more obvious during the first six months that he was on thyroid treatment.

The hair of the body may become scanty and lose its tendency to curl. Excessive growth of hair (hypertrichosis) in women after the menopause is an indication of disordered endocrine balance (loss of ovarian internal secretion ?) and is only so far an accompaniment of age; it may be seen in comparatively young women from various causes.

The nails are often longitudinally ridged, brittle, hard, and thickened; but onychogryphosis is rather the result of neglect or of disease than solely of old age.

The brain as a natural result of atrophy becomes lighter; Boyd's [2] tables show that

[1] Sinclair, J., *Code of Health and Longevity*, 1807, i. 68.
[2] Boyd, R., *Phil. Trans. Roy. Soc.*, 1861, cli. 241.

the male brain is 3 oz., and the female brain 4 oz., lighter in persons over 80 years of age than in the decade 20 to 30. The convolutions, therefore, become separated and the amount of cerebrospinal fluid greater. The atrophy is not uniform, being less in the posterior third than in the anterior two-thirds. The nerve cells become smaller, pigmented, and degenerate. The brain is said by Cerlette to be affected by a process special to old age—miliary necroses scattered over the cortex and associated with changes in the small arteries which show remarkable knots; a condition which suggests a pathological softening secondary to arteriosclerosis, especially as the change does not come on constantly at a definite age period. Cavities with thickened walls, possibly due to miliary haemorrhages, or to softening around the vessels are also described. Metchnikoff's description of phagocytic destruction of the nerve cells by macrophages has been seriously questioned and thought to be based on erroneous observation, the glia cells being regarded as macrophages (Marinesco).

The spinal cord shows an increased number of amyloid bodies, some diffuse sclerosis, often obliteration, by epithelial proliferation, of the central canal, and atrophy with pigmentation

of the nerve cells, especially in the anterior cornua. The membranes may contain small calcareous plaques.

The arcus senilis, due to infiltration with fats, especially cholesterol and lipochrome, and to degeneration of elastic tissue at the periphery of the cornea, is often associated with arteriosclerosis (Monauni[1]). It is not a necessary accompaniment of age ; among 321 persons over 80 years of age, it was absent in 114, or 35·5 per cent (Humphry) ; and it is well known that like grey hair, it may occur in those young in years. Nascher,[2] the author of *Geriatrics*, had an arcus senilis as a schoolboy. Rigidity and flattening of the crystalline lens lead to presbyopia, which may be premature and due to toxaemia, among the causes of which Ernest Clarke[3] gives intestinal toxaemia a high place. The power of accommodation is also impaired by weakness of the ciliary muscle brought about in the same way.

Skeleton.—The atrophy characteristic of senescence is well shown in the fixed tissues of the bony skeleton. Though the bones do not as a rule alter materially in size or shape,

[1] Monauni, *Arch. d'opth.*, 1921, xxxviii. 180.

[2] Nascher, I. L., *Geriatrics*, p. 36, 2nd edition, 1919, London.

[3] Clarke, Ernest, in *Operative Treatment of Intestinal Stasis*, by W. A. Lane, p. 245, 1918, London.

they do so markedly in substance from rarefaction and absorption, the latter taking place mainly from the inside of the bones and especially the cancellous tissue, the medullary cavity and the Haversian canals becoming larger (senile osteoporosis). Hence fractures near the joints, particularly intracapsular fracture of the neck of the femur, are favoured. The absorption of the alveolar border of the jaw is intimately connected with the loss of the teeth, and brings the mental foramen to the top of the edentulous mandible. The angle of the jaw at the junction of the body and the ramus now opens out and comes to resemble that of an infant. It is often stated that the angle of junction of the neck and shaft of the femur becomes less, more of a right angle, but Humphry regarded this as exceptional.

From muscular weakness the back becomes bent and as a result the vertebrae become altered in shape. Ossification of the anterior common spinous ligament—a change analogous to rheumatoid osteophytes around the more movable joints—is an added and not uncommon change but, like calcification of the costal and laryngeal cartilages, it is a morbid process, and when advanced constitutes spondylitis deformans. The intervertebral discs undergo

some loss of elasticity and atrophy, thus contributing to the loss of height. The cranial bones are usually thinned, and the parietal bones may show symmetrical or nearly symmetrical oval areas of excessive absorption of the outer and even of the inner table, so that the epicranium and the dura mater may be in contact. These areas which are close to the longitudinal fissure must not in the case of ancient skulls be mistaken for examples of early trephining. The bony sutures tend to become obliterated. Instead of thinning and loss of weight the skull, especially the vault, may show thickening and be heavier than normal—a change involving chiefly the inner surface and ascribed by Sir George Humphry to shrinkage of the brain.

Calcification of the costal and laryngeal cartilages, which have a yellow tint from fatty change, is, like a similar change in the arteries, pathological and not part of the process of senescence. Thus among 10 recorded necropsies on centenarians the costal cartilages were calcified in 2 only. Calcification of the costal cartilages interferes with the respiratory movements and was regarded by Sir George Humphry, who tested for it by estimating the elasticity perceived when gentle pressure is

exerted on the lower part of the sternum, as a bad omen for the future.

The teeth are usually, but not invariably, few in the aged, for care or lack of it, the accumulated effect of long-continued mechanical injuries, altered calcium metabolism, and diminished resistance to infection will necessarily influence the amount of decay. Statistics, especially Humphry's, show that in extreme old age very few teeth are present, and it is tempting to correlate the diminished provision for mastication with the lessened need for food. Sir Isaac Newton, however, at the age of 85 was said to have lost one tooth only. The numerous reputed instances of a third dentition can be explained only by the appearance of a previously buried tooth through the atrophying gums, for a genuine third dentition would necessitate the presence of dental germs which do not exist.

The gastro-intestinal tract shows atrophy of the muscular coat and its secreting glands, so that dilatation of the thin-walled, pale stomach and colon occur on less provocation than in adult life and digestion is impaired ; from lack of mucous secretion combined with loss of motor vigour constipation is common. It may be added that hypertrophy of the prostate

by interfering with peristalsis of the colon has been thought to cause gerontal constipation (Hollis [1]). The pancreas shows fibrotic atrophy and becomes smaller and harder. From the loss of fat and muscular atrophy visceroptosis is not uncommon.

The liver diminishes in size and weight by about one half ; atrophy of considerable areas may expose the vessels and ducts on the surface of the organ. Boyd's tables show a difference of 18 oz. between the weights in persons in the decade 20–30 and in those over 80. Microscopically atrophy of the lobules and of the cells in the centres of the lobules have been described (Luciani [2]), but the latter change is not constant, for in a woman of 93 Salimbeni and Gery [3] definitely noted that the cells were not atrophied. That such atrophy of the liver cells is pathological is perhaps supported by D. Symmers's [4] observation that in the pancreas of such cases the islands of Langerhans may show moderate enlargement, as if to compensate for failure of the glycogenic function of the liver. Pigmentation of the cells by a

[1] Hollis, W. A., *Brit. Med. Journ.*, 1916, i. 677.

[2] Luciani, *Text-book of Physiology*, English translation, vol. v. p. 302, London.

[3] Salimbeni et Gery, *Ann. Inst. Pasteur*, Paris, 1912, xxvi. 577.

[4] Symmers, D., *Arch. Int. Med.*, Chicago, 1909, iii. 270.

lipochrome is excessive, and the name brown atrophy has been applied to the condition which is seen in the other viscera of the old.

The lungs become smaller, lighter, and the elastic tissue degenerates ; this is atrophous emphysema, and the chest capacity diminishes. Roussy and Leroux[1] found that these lungs commonly show endarteritis obliterans and fibrosis, conditions which favour infarction, infection, and the terminal bronchopneumonia to which the aged are so prone.

The voluntary muscles, according to Durante,[2] contain many fibres with large globules of fat ; but Jewesbury and Topley,[3] who describe coarse fat globules mingled with brown pigment in the immediate neighbourhood of the muscle nuclei in 50 per cent of cases of various kinds, and almost constantly in old subjects, regard this condition as independent of true fatty degeneration, and are doubtful if it has any pathological significance. Excessive fatty and fibrotic change is found in cases of senile paraplegia without any lesion in the spinal cord or brain.

Heart.—Some difference of opinion exists

[1] Roussy, G., et Leroux, R., *Ann. de méd.*, Paris, 1921, ix. 161.

[2] Durante, *Manuel d'histologie pathologique* (Cornil et Ranvier), 1902, ii.

[3] Jewesbury and Topley, *Journ. Path. and Bacteriol.*, 1913, xviii. 432.

as to the condition of the heart ; Parkes Weber [1] says that the only true senile change is diminution in size and weight ; this as it is worded is no doubt correct ; but pure atrophy is less rare in the heart than in most parts of the senile body. Charcot [2] indeed stated that it does not atrophy in old age, but preserves the dimensions of middle life. The heart may even hypertrophy in old people ; this is pathological ; Councilman [3] found it in 248, or 43 per cent, of 580 persons over 60 years of age, and could not refer it to aortic or renal arteriosclerosis or to the diminished capillary area in the skin ; but the average blood pressure $\frac{158 \text{ systolic}}{88 \text{ diastolic}}$ of the cases with cardiac hypertrophy was higher than that $\frac{130}{78}$ of the others.

Fatty degeneration of the myocardium is very frequent ; Charcot stated that at the Salpêtrière it was almost constant in old women, but according to Councilman there is no clear evidence that it produces permanent injury or functional insufficiency ; he noted some fibrosis

[1] Weber, F. P., *System of Medicine* (Allbutt and Rolleston), 1905, i. 185, London.

[2] Charcot, J. M., *Clinical Lectures on Senile and Chronic Diseases*, p. 28, New Sydenham Soc., 1881.

[3] *Loc. cit.*

in 15 per cent of his cases. Atrophy of the epicardial fat—serous atrophy—is common, and increase of the so-called lipochrome pigment in the muscular fibres which become smaller and fewer—brown atrophy—is frequent as it is in the other organs in old age.

Chronic valvulitis and subendocardial fibrosis are, like arteriosclerosis, common morbid changes.

Arteriosclerosis, contrary to what has been stated by Huchard and others, is not constant in a considerable degree in old people, and therefore cannot, as Demange and others considered, be regarded as the cause of the atrophic changes seen in old age. Arteriosclerosis is due to several factors, namely, infection and intoxication of various kinds and to damage caused by long-continued high arterial blood-pressure. The primary changes are degeneration and weakness, however brought about, in the middle coat. Ophülz [1] has recently discussed the question whether the degeneration is entirely or largely a senile change ; if it were so, the curve of the incidence of arterial sclerosis would begin gradually about the age of 40 years, so as to include premature cases, and

[1] Ophülz, W., *Stanford Univ. Publications, Med. Sciences*, 1921, vol. i. Part I. p. 31.

rise slowly until the age of 55 years, when there would be a sudden increase to 80 or 90 per cent, and at the age of 70 it would be improbable that any one would be free from well-marked arteriosclerosis. He found that the curve of incidence was very different from this; beginning much earlier its rise is gradual all the way without any sudden increase, and indeed seems, if anything, to be retarded by old age. Old persons may have practically healthy arteries, so, although arteriosclerosis may undoubtedly produce atrophy and senile changes in the tissues and organs by diminishing the blood-supply, for example in the case of the red granular kidney, it cannot be regarded as the causal factor in healthy old age.

The primary calcification of the middle coat, sometimes called Mönckeberg's sclerosis, which leads to the formation of regular rings in the degenerated muscular media and the "pipe-stem" arteries associated with senile gangrene, may be independent of, or combined with, endarterial sclerosis. It follows fatty degeneration of the media, which is the commonest form of medial degeneration in the aged, and specially picks out the elastic fibres.[1] The femoral, tibial, radial arteries and the aorta are

[1] Turnbull, H. M., *Quart. Journ. Med.*, Oxford, 1913–14, viii. 201.

most often affected. It is difficult to estimate its incidence, but that it is not very common, at any rate in a high degree, seems probable from the comparative infrequency of its detection in *x*-ray examinations of the lower limbs in old people. It would be natural to associate its occurrence with the rarefaction of bone that goes on in advanced life, and so to consider it as in some respects different from the secondary calcification in endarteritic sclerosis ; in answer to an enquiry Professor W. T. Councilman of Harvard kindly wrote to me that he did not regard calcification as characteristic of any particular type of arterial disease, lime salts being in certain cases more easily deposited in any pre-existing lesions. Klotz describes fatty and calcareous change in the middle third of the media of the aorta as quite characteristic of senescence.

Cazalis's famous aphorism " man is as old as his arteries " is true in so far that the state of the arteries is a good index of the general condition, for they are extremely prone to suffer as the result of infection, toxaemia, and strain ; strictly speaking, therefore, the state of the arteries is not so much an index of the individual's age as of his adventures.

Phlebosclerosis, analogous to arteriosclerosis,

is common, and dilatation, often due to stagnation and lack of the normal *vis a tergo*, of the veins is a familiar change in the aged.

The capillary area is diminished in the skin and elsewhere, but not uncommonly there are dilated venules or angiomas on the skin ; the latter, commoner on the trunk and upper limbs and in men, were formerly known as " de Morgan's spots " and were thought to accompany cancer, but the association is only due to a rough correspondence of their age incidence.

The blood of healthy octogenarians may not show any departure from that of the earlier periods of life as regards the number of the reds and the amount of haemoglobin (Hansen [1]), though some have described a secondary anaemia. Thus in a female centenarian Macnaughton [2] found slight secondary anaemia with a normal number of leucocytes, the differential count showing a relative lymphocytosis. The red bone marrow diminishes, its place being taken by fat cells.

The lymphoid tissues undergo atrophy all over the body including the leucoblastic bone marrow, but though it does not appear that the blood shows any definite change in the leucocyte

[1] Hansen, K. M., *Ugsek. f. Laeger*, Copenhagen, 1919, lxxxi. 1281.
[2] Macnaughton, F. G., *Brit. Med. Journ.*, 1922, ii. 14.

count it is tempting to correlate the diminution of resistance to acute infections, such as pneumonia and erysipelas, with the atrophy of the lymphoid tissue. The alimentary canal often shows lymphoid atrophy in a high degree, but two normal Peyer's patches were present in a man reputed to be 106 years old (G. Rolleston[1]).

The spleen, in common with the lymphoid tissues elsewhere, shows atrophy, sometimes to an extreme degree, so that instead of the normal weight of 7 oz. it weighs a few drams only. The capsule is thrown into folds, and is somewhat opaque ; from atrophy of the pulp and Malpighian corpuscles the vessels and fibrous trabeculae become prominent. *The thymus*, contrary to the general opinion that it undergoes involution long before puberty, has been found by Hammar [2] to increase in size up to puberty when involution begins, but proceeds so gradually that even in old age it is functional.

The *thyroid*, unless there is cystic change, is smaller than natural ; thus out of 40 thyroid glands from individuals between the ages of six months and 77 years the smallest was in a woman aged 77 (Hale-White [3]). In colour it

[1] Rolleston, G., *Brit. and For. Med.-Chir. Rev.*, 1863, xxxi. 505.
[2] Hammar, A., *Endocrinology*, Los Angeles, 1921, v. 543.
[3] Hale-White, W., *Med.-Chir. Trans.*, 1888, lxxi. 181.

is darkish brown and on section rather dry. Dr. Donaldson, Lecturer on Pathology at St. George's Hospital, has specially examined 19 thyroid glands from patients between the ages of 57 and 93 ; of these five showed cystic change ; they all showed increase in the amount of fibrous tissue which was progressive with age, and in the absence of cystic change the size of the vesicles and amount of colloid material were diminished.

The Parathyroids.—From examination of a number of specimens Dr. Donaldson finds that in old people the parathyroids appear to be free from retrogressive changes, but he cautiously requires further experience before concluding that this is the rule.

The *adrenals* show involutionary atrophy in common with the body as a whole, but sometimes the cortex is enlarged from excess of lipoids, usually associated with considerable atheroma, and may also show adenomas. As the increase in size of the adrenals is cortical its relation to high blood pressure, if any, is that of a remote result, namely from arteriosclerosis, and not causal as has been suggested. According to G. M. Findlay[1] the amount of lipo-

[1] Findlay, G. M., *Journ. Path. and Bacteriol.*, Cambridge, 1920, xxiii. 482.

chrome in the cells of the adrenals increases with advancing years and is accompanied by the appearance of melanin in their nuclei.

The *kidneys* show definite atrophy, and Councilman,[1] who has recently made a study of them in 580 persons over 60 years of age, calls the condition chronic atrophic nephropathy. The fat in the renal pelvis is more obvious than usual, the capsules are slightly thickened and occasionally but by no means always adherent, the surface finely rough and sometimes showing small cysts, but the large and irregular depressions characteristic of a granular kidney are not common. There are, however, areas of fibrosis, and the cortex and medulla are equally atrophied. Microscopically some glomeruli are fibroid, others smaller than natural. In three-fourths of his cases the renal vessels showed arteriosclerosis due to primary atrophy of the media with compensatory hypertrophy of the intima ; but Councilman gives reasons for hesitation in accepting the obvious conclusion that the senile kidney is the result of the vascular change.

The prostate shows some degrees of enlargement after the age of fifty in the vast majority

[1] Councilman, W. T., *Contributions to Medical and Biological Research*, Dedicated to Sir William Osler, 1919, vol. ii. p. 919, New York.

of men, but in only a percentage of these are there symptoms referable to it. Kenneth Walker[1] finds that the maximum size is reached at the age of 60 and that from then onwards there is a slow diminution in size ; among 340 men between 80 and 90 there were 11, or 3·2 per cent, and among 92 men between 90 and 100 one only with hypertrophy of the prostate (Humphry). The causation of prostatic hypertrophy has been much discussed ; that its association with arteriosclerosis (Launois[2]) is anything more than a coincidence, the two conditions being common in the later years of life, seems improbable ; Walker found the two associated in 10 per cent, and he regards the change as part of a general enlargement and thickening of the peri-urethral, sub-cervical, and sub-trigonal glands, and, as the interstitial cells in the testes become fewer and degenerated, he considers that the prostatic enlargement is possibly a degeneration connected with a disturbance of the endocrine balance. Nemenow[3] argued that prostatic enlargement was due to proliferation of the interstitial cells following senile atrophy of the seminal tubules of the

[1] Walker, K., *Brit. Med. Journ.*, 1922, i. 297.

[2] Launois, "Appareil urinaire des vieillards," *Thèse de Paris*, 1885.

[3] Nemenow, M., *Ztschr. f. Urol.*, Berl. und Leipz., 1921, xv. 45.

testes, but K. Walker found that in prostatic enlargement the interstitial cells are diminished rather than increased in number. An interesting parallel has been drawn between the involutionary changes in the mamma and the prostate, and it is probable that the same underlying factor is at work in both (Walker, Paul). Hertoghe[1] regarded some cases of prostatic hypertrophy as due to senile dysthyroidism, and recently benefit has been reported from thyroid medication and also from prostatic extract. Dr. Leonard Williams has told me of cases, as yet unpublished, showing well-marked relief of symptoms and diminution in the size of prostatic enlargement after doses of thyroid extract (½ grain once) and colloidal iodine (one dram three times) daily. The prostatic plexus of veins is often enlarged and may contain phleboliths.

The *testes* become smaller, softer, and commonly show some atrophy of the tubules with disappearance of the epithelial lining and thickening of the basement membrane; but the testes of old men may be free from any such change and the spermatozoa in the vesiculae seminales may be active. According to K. Walker the interstitial cells gradually

[1] Hertoghe, "L'Hypothyroidie bénigne chronique," *Bull. Acad. roy. de Belg.*, 1899.

diminish in number from the age of 30, but they may be present in men over 80, and Mott [1] remarks that their persistence may account for an increased and perverted sexual appetite, due to stimulation of the desire without the power to perform the sexual act.

The *penis* becomes smaller, often retracted, the *glans* harder, and the *scrotum* smaller.

The *ovaries* become shrivelled and fibrotic ; the ova disappear or small cysts may form. It is difficult to find statements about the presence or absence of interstitial cells in the senile ovary. Professor Turnbull has kindly informed me that in old women an occasional cell which might be, but is not certainly, an interstitial cell is visible, and that if they are interstitial cells their number must be small and their development poor.

The *uterus* becomes small, its cavity round, and the cervical canal may be obliterated. The *external genitals* atrophy.

The *mamma* in women shows involution changes and when excessive (cystic disease) these may, as Paul [2] has pointed out, be compared with prostatic enlargement in the male.

[1] Mott, F. W., *Brit. Med. Journ.*, 1919, ii. 658.
[2] Paul, F. T., *Lancet*, 1910, ii. 294.

VII

PHYSIOLOGY OF OLD AGE

THE basis of the physiology of old age is progressive diminution in functional activity, which corresponds to the characteristic structural atrophy of the organs and tissues. Thus the lowered functional activity of its glands is manifest in the dry skin ; according to Haneborg [1] there is usually a fall in the percentage of hydrochloric acid in the gastric juice, though Bell [2] disputes this. The lessened amount of mucus from the intestine probably plays some part in the tendency to constipation. Other evidences of lowered metabolic rate are seen in the diminished efficiency of the acid-base equilibrium (MacNider [3]) and the increased degree of urea-nitrogen in the blood, as shown in 50 per cent of 41 persons between 70 and 88 years of age examined by Rappleye.[4]

[1] Haneborg, *Acta Medica Scandinavica*, 1921, Supplement I. p. 117.
[2] Bell, *Lancet*, 1922, i. 715. [3] MacNider, *Science*, 1917, xlvi. 643.
[4] Rappleye, *Boston Med. and Surg. Journ.*, 1918, clxxviii. 191.

Temperature.—Before the era of the clinical thermometer it was supposed that the body temperature of the aged was below normal. This belief was part of the ancient view that the cause of old age was exhaustion by the natural heat of the radical moisture which, like lamp oil, supported the innate heat and with the passage of years could not be supplied as perfectly as before ; as a result of this loss of radical moisture the body was thought gradually to dry and cool.[1] But it is now known that the internal temperature is almost constant at all ages, and Charcot proved that the only real difference is that the axillary is lower than the rectal reading ; this is due to the diminished vascularity of the skin and to the corresponding fall in the loss of heat, which again may be correlated with the lower metabolic rate of old age. Aub and Dubois'[2] observations on six men between 77 and 83 years of age, mainly with arteriosclerosis, granular kidney, and emphysema, showed that

[1] *A Discourse Of The Preservation Of The Sight : Of Melancholic Diseases : Of Rheums and Of Old Age*, composed by M. Andreas Laurentius, Ordinarie Phisition to the King and Publike Professor of Phisicke in the Universitie of Montpelier. Translated out of the French into English according to the last Edition by Richard Surphlet, Practitioner in Phisicke, p. 170, London, 1599.

[2] Aub and Dubois, *Arch. Int. Med.*, Chicago, 1917, xix. 823.

the basal metabolism was 12 per cent below the average for men between 20 and 50.

Blunting of sensibility to pain is a beneficent process, suggesting that with the gradual process of involution and approach to a physiological death the need for the warning normally conveyed by symptoms is no longer needed. This is connected with the simultaneous atrophy of the nervous tissues which look after the conduction, perception, and reference of pain. The latency of disease, as shown by an absence of the characteristic symptoms observed in earlier adult life, is often remarkable in the aged. Thus death may occur suddenly from extensive but entirely unsuspected pneumonia ; the passage of biliary or urinary calculi may be unaccompanied by the violent colic of these events in ordinary cases, and extensive malignant disease may exist without any definite localizing discomfort. This failure in the power to react is also shown in fevers and infections (*vide* p. 142).

Cutaneous sensation is little affected, and indeed the aged are very sensitive to cold. Taste and smell are impaired, and presbyopia is due to changes in the crystalline lens. The pupils are contracted and the iris sluggish. From weakness of the orbicularis palpebrarum

muscle ectropion and epiphora may noticeably change the facial appearance. With advancing years hearing commonly becomes less acute from various causes, and after 60 there is a successive decrease in the number of persons with normal hearing. According to Albert Gray [1] there is probably a characteristic form of deafness for the higher notes of Galton's whistle in all old people, even when for all practical purposes there is no obvious defect or tinnitus ; this he regards as due to progressive atrophy of the ligamentum spirale. Chronic progressive labyrinthine deafness, due to atrophy of the auditory nerve and fibrosis of the ductus cochleariae, is the most common condition in persons over 60. Fixation of the stapes frequently causes deafness, and the sequels of middle-ear disease accumulate with advancing years. Gouty eczema of the external auditory meatus and collections of wax may seriously interfere with hearing. Tinnitus in the elderly is commonly associated with high blood pressure and arteriosclerosis.

Appetite for food is sometimes capricious ; old people may eat excessively, possibly because the pleasures of the table are the only ones to which they feel equal.

[1] Gray, A. A., *Diseases of the Ear*, p. 335, 1910.

Muscular movement is slow and somewhat uncertain, and the reflexes are diminished except in the presence of sclerosis of the spinal cord. According to Moebius the *knee-jerk* is often absent in normal old persons, but Sternberg, by employing methods of reinforcement not available in Moebius' time, found that it was invariably present even in the tenth decade.

The *sleep* of the aged is less continuous, and from interruptions often appears to them to be much less than it really is. There is often a tendency to irregularity, bad and good nights alternating. But too much attention to disturbed sleep in the aged must be avoided, as hypnotics are inadvisable, and it has been urged by Sir Hermann Weber and others that too much sleep is more harmful than too little.

In old age the *mental condition* varies in different individuals according to their previous character and their present physical state. Freedom from sexual and other perturbations often renders the minds of old people calm, tolerant, less susceptible to disappointed ambition, and philosophic when the part of spectator has been accepted in place of that of actor in life's drama. In what may be regarded as normal old age psychical activity diminishes ;

not only do initiative, elasticity, and originality fail, but new ideas and fresh lines of thought are assimilated with difficulty ; hence the old are commonly conservative and *laudatores temporis acti*. Mental fatigue occurs more readily and the power of concentration and attention is impaired so that the old may appear deaf ; the mind begins to show disintegration and a return to the primitive condition in which each act demands individual care ; it has indeed been said that old age is nothing but progressive fatigue. A less agile memory for names is commonly one of the early symptoms of senescence, and long precedes the characteristic loss of memory for recent events while that for the remote past remains, as if the nerve cells were photographic plates which in course of time have all become occupied with impressions. With commencing failure of memory there is often a tendency to make the same remark or tell the same story repeatedly, to mislay things, and unconsciously to become careless about personal appearance and habits. As a kind of protest against the inevitable there may, in the early stage of old age, be a tendency to ape the young and to conceal the true age ; thus a man may remove the date of his birth from *Who's Who* and books of reference, and

a mother may delay the " coming-out " of her daughter. On the other hand, at a later stage there may be the opposite desire to appear a wonderful prodigy of senescence. The old are notoriously less subject to feel the loss of relatives and friends by death ; they become more self-centred ; this may be because retirement from active work switches their minds on to their own feelings, and possibly in part depends on loss of touch with the external world, resulting from failure of the sense organs. This when exaggerated develops into selfish dependence and demands on relatives. Senile vanity is not uncommon, and Eden Phillpotts[1] remarks that all old people love to be in the centre of the stage, one of the pathetic things in life being that they are seldom allowed to be there. The ego-centric frame of mind may lead to hypochondriasis with fads and meticulous attention to details of personal health and to experiments in diet and patent medicines. Loss of control, due to failure of the higher centres, engenders restlessness, garrulity, emotional weakness, and peevishness. There may be considerable variation in the moods, so that the deep depression of one day may vanish the next, and irritability and apathy may alternate.

[1] *The Gray Room*, p. 261, 1922.

Regression, which closely corresponds to the "devolution" of Hughlings Jackson, who argued that in disease the organism tends to retrace the steps of its development, accounts for the phenomena of "the second childhood." Thus the old are prone to nervous apprehension, and liable to suggestion and to hysteria which Rivers[1] defined as a protective mechanism representing a recrudescence of the reaction to danger in an early stage of animal development. Will power, like their gait, becomes hesitant and uncertain. This devolutionary change progresses partially and not universally; memory for personal names, as mentioned above, is often the first to fail, because, like the mathematical faculty, it has from the attendant difficulty a high place in the order of mental processes; hence forgetfulness of personal names is a criterion of psychical fatigue and neurasthenia (Dupuis[2]).

In old animals it is natural for the instinct of self-preservation to fade, as is exemplified in the day-flies which in their larval stage are well endowed with this property, and as their end draws near animals seem to acquire an

[1] Rivers, W. H. R., *Instinct and the Unconscious*, p. 148, 2nd edition, Cambridge University Press, 1922.

[2] Dupuis, *Journ. de psychol.*, Paris, 1921, xviii. 481.

instinct for death comparable to that for sleep. But in human beings, although they usually dislike old age, there is generally what Matthew Arnold [1] called " a passionate, absorbing, almost bloodthirsty clinging to life." Metchnikoff specially investigated this point and found hardly any instances in which death was anticipated with the same feelings of pleasure as is sleep by the weary. Considering the discomforts of many old people it is rather remarkable how very seldom they endorse the words of the burial service : " We give thee hearty thanks for that it hath pleased thee to deliver this our brother out of the miseries of this sinful world." Various explanations have been offered for this want of harmony between the mental and physical states of the old ; it has been ascribed to the idea of eternal punishment, and to the presence of pathological conditions which bring on senility and death prematurely and thus alter what should be the normal mental attitude of healthy old age. In speaking of the usual fear of death in old people it should be mentioned that shortly before death this commonly disappears and, as G. E. Day,[2] R. W. Mackenna,[3] and Thompson

[1] Arnold, M., *Essays in Criticism*, Preface, p. x. 1886.

[2] Day, G. E., *Domestic Management and Diseases of Advanced Life*, p. 5, 1849, London. [3] *The Adventure of Death*, p. 63, 1916, London.

and Todd point out, the aged when seriously ill commonly regard death as a welcome release ; the famous William Hunter's last words in his sixty-fifth year expressed his sense of resignation : " If I had strength enough to hold a pen, I would write how easy and pleasant a thing it is to die."

The Cardio-Vascular System.—The pulse rate is usually rather increased in frequency as compared with that in adult life ; extra-systoles are so common in persons who appear otherwise normal that they cannot be regarded as having any important significance. Among Sir George Humphry's collection of 824 persons over 80 years of age one-fifth had an irregular or intermittent pulse.

Although, like arteriosclerosis, a well-marked high blood pressure without evidence of renal disease, to which Sir Clifford Allbutt has given the name of senile plethora or hyperpiesia, is common in the decline of life, it is a pathological and not a physiological change ; and a distinction must be drawn between the gradually rising blood pressure seen from birth onwards and an increase above that normal to an arterio-vascular system that has been active for over half a century. In the same way the venous pressure increases with

age (Hooker[1]). That a definitely high blood pressure in the aged is pathological appears to be shown by observations quoted by Councilman from the Peter Bent Brigham Hospital, Boston ; among 94 patients (male and female) averaging 66 years of age, 44 per cent with cardiac hypertrophy as shown by necropsy, had an average blood pressure of $\frac{158 \text{ systolic}}{88 \text{ diastolic}}$, whereas the 56 per cent without cardiac hypertrophy had an average blood pressure of $\frac{130}{78}$. In both series the differences between males and females were never more than 7 mm. Hg. From observation of 102 Chelsea pensioners over 75 years of age Thompson and Todd found that the average blood pressure was $\frac{145 \text{ systolic}}{80 \text{ diastolic}}$, estimations varying from $\frac{190}{100}$ to $\frac{115}{70}$, and that the average pulse pressure, or difference between the systolic and diastolic pressures, was 67 mm. They came to the conclusion that it was not possible to arrive at a normal blood pressure for old people on account of the varying conditions of the heart and arteries.[2]

[1] Hooker, D. R., *Amer. Journ. Physiol.*, 1916, xl. 43.
[2] Thompson, R. J. C., and Todd, R. E., *Lancet*, 1922, ii. 503.

The urine, in consequence of the lowered metabolism and general atrophy, is somewhat diminished in quantity with a fall in the solids, though the specific gravity remains about normal. The chlorides are stated to be normal and the phosphates and urea to be diminished. Slight glycosuria as a result of a low sugar tolerance (*vide* Spence[1]) is not uncommon, especially in obesity. Prolonged confinement to bed has been thought to be responsible for casts in the urine. A trace of albumin is not rare; this may be due to various factors, and in itself is not a cause for anxiety; but a well-marked fall in the specific gravity is a sign of renal inadequacy which may be preceded and anticipated by the discovery of nitrogen retention in the blood.

Sexual activity in man wanes generally speaking after 50, but there are great variations in this respect, and sometimes there are periods of considerable excitement in old men, often thought to be associated with prostatic enlargement.

It would naturally be expected that *wounds* and *fractures* of bones would heal more slowly in the old than in the young, and, according to Carrel and Ebeling,[2] the cicatrization of

[1] Spence, J. C., *Quart. Journ. Med.*, Oxford, 1920-21, xiv. 314.
[2] Carrel and Ebeling, *Journ. Exper. Med.*, Baltimore, 1921, xxxiv. 599.

human wounds varies inversely, if accurately measured, with the age of the patient; Humphry, however, found that, provided sloughing did not occur, wounds and ulcers in the aged heal as quickly as in middle life, and that the failure of union in intracapsular fracture of the neck of the femur is due to want of apposition and not to the age of the patient.

In some respects the *reaction to drugs* in the senescent body is different from that in ordinary adult life. In old people absorption from the alimentary canal is slow and this is particularly so with gelatin-coated pills and drugs, such as cinchona, containing tannin, which should therefore be avoided. The physiological response to drugs is slower and more prolonged than in early life, so that for this reason and from the frequency of constipation an accumulated action is thought to be more likely to occur in the aged. It is sometimes said that large doses are not borne well by the old and that morphine is dangerous as it is in infants, but Nascher [1] states that if, in order to obviate the paralysing effect of morphine on a weakened respiratory centre, atropine is given before the morphine so that their action can be timed to coincide, instead

[1] Nascher, I. L., *Geriatrics*, p. 60, London, 1919.

of giving them at the same time when the effect of the atropine comes later, morphine can be given in the same doses as in maturity. Purgatives may be required in larger doses than in ordinary practice. According to Leonard Williams [1] bromides are likely to produce mental confusion in old people and if persisted in, even in ordinary doses, may be followed by vascular thrombosis and permanent impairment of the intellectual powers. Sedatives and hypnotics when necessary should be given in small doses and discontinued as soon as possible ; but they may be necessary for restlessness which would otherwise seriously exhaust the failing strength.

[1] Williams, L., *Minor Ailments*, p. 332, 1920.

VIII

THE DESCRIPTION OF OLD AGE IN THE TWELFTH CHAPTER OF ECCLESIASTES

When first approaching the subject of old age every one must recall the famous description in the first six verses of the twelfth chapter of Ecclesiastes beginning "Remember now thy Creator in the days of thy youth while the evil days come not, nor the years draw nigh when thou shalt say I have no pleasure in them." Formerly ascribed to King Solomon (977 B.C.) the book of Ecclesiastes (in Hebrew Koheleth = the preacher) has been shown by the higher criticism to date only from the end of the third century B.C., and from internal evidence, namely references to the brain, spinal cord, and other anatomical structures, though expressed with poetic imagery, it may fairly be assumed

that a medical man was concerned with its construction. In his attractive work, *A Gentle Cynic*,[1] the late Professor Morris Jastrow, jun., of Philadelphia explained that the book of Ecclesiastes as it appears in the authorized version, consists of (i.) the original, cynical, but good-natured *obiter dicta* of the unknown dilettante who preferred to veil his identity under the name of Koheleth, and (ii.) additions and modifications made by various hands to render it more orthodox and compatible with the tradition that it was written by Solomon; thus the admonition "of making books there is no end and much study is a weariness of the flesh" may very probably have been intended as a hint that Koheleth's views should not be taken too seriously. Following this conception Jastrow reconstructed the text of the book of Ecclesiastes to what he argued was its original form, and compared it with the more modern writings of Omar Kháyyám and Heinrich Heine. As we all must have speculated over the correct interpretation of the various metaphors in this description of the last stage of life, the explanations offered by others, such

[1] *The Gentle Cynic, being a Translation of the Book of Koheleth, commonly known as Ecclesiastes, stripped of later Additions, also its Origin, Growth and Interpretation*, by Morris Jastrow, junior, 1919, J. B. Lippincott Co.

as Andreas Laurentius (1599),[1] Master Peter Lowe (1612),[2] founder of the Faculty of Physicians and Surgeons of Glasgow, Bishop J. Hall (1633),[3] John Smith (1665),[4] Richard Mead (1775),[5] and Jastrow may be very briefly mentioned. The second verse, "While the sun, or the light, or the moon, or the stars, be not darkened, nor the clouds return after the rain," is regarded by Laurentius, Lowe, and Hall as referring to the ocular disabilities of old age, whereas Smith and Mead consider that mental failure and depression are meant. As regards the third verse, "In the day when the keepers of the house (the hands) shall tremble, and the strong men (the legs) shall bow themselves (become bent), and the grinders (teeth) cease because they are few, and those that look out of the windows (the eyes) be darkened," there is general agreement, Lowe specially designating cataract as meant in the last sentence. "And the doors shall be shut in the

[1] Laurentius, A., *A Discourse of the Preservation of the Sight; of the Melancholic Diseases; of the Rheums; and of Old Age*, translated out of French into English by Richard Surphlet, 1599.

[2] Lowe, P., *The Whole Course of Chirurgerie*, 1612.

[3] Hall, J., *Paraphrase upon the Hard Texts of the Whole Divine Scripture*, 1633.

[4] *Loc. cit.*, *vide* p. 8.

[5] Mead, R., *Medica Sacra*, translated from the Latin by Thomas Stark, 1775.

streets," is regarded as referring to the mouth by Laurentius and Mead, and to the various orifices including the results—constipation and dysuria—by Smith ; " when the sound of the grinding is low," is considered by Jastrow to mean impaired hearing, and by Smith as a lowered rate of metabolic processes, such as assimilation, blood formation, and various secretions. " And he shall rise up at the voice of the bird," implies, according to Smith and Mead, the early waking of the elderly ; " and all the daughters of music shall be brought low " signifies to Laurentius the failure of voice, to Mead deafness, and to Smith all the organs concerned with sounds, namely the lips, tongue, larynx, and the auditory apparatus. " Also when they shall be afraid of that which is high, and fears shall be in the way " is regarded by Smith as describing the general mental attitude of anxiety for things both small and great and a bad head for height, but a more modern commentator suggests that " afraid of that which is high " refers to dyspnoea on climbing a hill. " And the almond tree shall flourish " is by Laurentius, Hall, and Smith thought to refer to the white hair or " churchyard flowers " of the old, but Mead argued that loss of smell is meant. " And the grass-

hopper shall be a burden" has been very variously interpreted : Hall is content to accept the literal meaning that the least weight is a nuisance ; Laurentius and Lowe understand oedema of the legs ; John Smith that the aged body undergoes the reverse change of shrivelling, hardening, and angularity ; Mead suggests scrotal hernia, and Jastrow, as according to the Talmud the grasshopper is a symbol for the male sexual organ, considers that the sentence refers to the loss of sexual activity. In the sixth verse the words " Or ever the silver cord be loosed," refers, according to Laurentius, Lowe, Mead, and Jastrow, to kyphosis, but Smith translates them into paralysis of the spinal cord and nerves. " Or the golden bowl be broken," signifies cardiac failure to Laurentius and Lowe, but cerebral haemorrhage to Smith, who thus explains the next line, " or the pitcher (the veins) be broken at the fountain (the right ventricle), or the wheel (the arterial circulation) broken at the cistern" (the left ventricle), and therefore concludes that King Solomon was perfectly acquainted with the circulation of the blood discovered by William Harvey in 1616. " The pitcher " is regarded as the vena cava by Laurentius, and as the urinary bladder by Mead and Jastrow ; " the

wheel broken at the cistern" suggests the kidneys and bladder to Laurentius and Lowe, cardiac failure to Mead, and intestinal and hepatic insufficiency to Jastrow.

IX

DISTINCTION BETWEEN HEALTHY AND MORBID OLD AGE

In any individual instance the exact line which separates healthy old age (senescence) from old age complicated by a morbid process, *i.e.* by some factor other than the gradual atrophy and restriction of functional activity, or senility, may be difficult or impossible to draw. The dictum of Terence, Cicero, and Sanatorius that old age is a disease probably still finds acceptance with many. It is indeed clear that exposures to infections and poisons would produce changes more easily in cells that are beginning to fail in vitality. Healthy old age should be a normal process of involution with progressive atrophy and loss of vitality, and free from any morbid change due to other factors whether extrinsic, such as infection, or intrinsic and due to abnormal metabolism. As the bodies of the aged usually show a number of changes

additional to those of normal involution, some of which, such as arteriosclerosis, are so frequent that they have sometimes been erroneously regarded as part or even the cause of old age, it is essential to recognize and to try to draw a distinction between physiological old age and senility from the effects of disease (*Senium ex morbo*). But about the anatomy and physiology of normal old age much remains to be learnt ; more indeed is known about the pathology of the aged, a subject which includes the damage done in the past, perhaps in youth, and morbid processes starting during advanced life.

In attempting to decide when old age should be regarded as a disease or merely as a process of involution or retrogression which naturally follows the earlier and progressive stage (youth) of development, it may be well to refer to the meaning of "disease" and "health." Disease, or want of ease, has been variously defined as evidence of imperfect function, as discord, and as maladjustment between the individual and his environment (Moon [1]), and Health as the indication of perfect functional activity, as harmony between the individual and his environment. In the different stages of life's

[1] Moon, R. O., *The Relation of Medicine to Philosophy*, p. 217, 1909, London.

cycle there should be a correspondence between the individual's desires and his powers so that there is harmonious co-ordination ; this should hold good in normal old age as it does in youth.

The frequent complaints of old people show that there is maladjustment and disease, for if the decline of vitality were uniform throughout the body the equilibrium would, though altered as a whole, still be maintained, and there would no longer be a discordant desire for activity, for which other parts of the body are, from a more advanced state of atrophy or morbid change, unable. Thus it would appear that the conscious disabilities of old age are not the necessary results of a true physiological involution, and that the late Sir Andrew Clark's definition of Old Age as " the period at which a man ceases to adjust himself to his environment " should be regarded as true of senility or morbid old age but not of senescence or healthy old age.

The organs of the body do not all start to grow old at the same time or progress at the same time. That such variations in involution may be so exaggerated as to become morbid without any very obvious cause is highly probable, but the latter event is clearly a departure from the progress of normal old age. The

precocious atrophy of some tissues or organs may be ascribed to several factors, such as inherent weakness, the effects of overstrain, though without producing gross changes, or to the influence of a definite infection or intoxication in the past. Thus deafness may be hereditary, senile paraplegia has been known to occur in energetic walkers, and thyroid deficiency may be the outcome of a past attack of enteric fever. These errors in the chronometry of life, as Sir James Paget [1] termed the different ageing of organs, cannot be regarded as a physiological process.

[1] Paget, J., *Studies from Old Case Books*, p. 93, 1891, London.

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X

DISEASES IN AND OF OLD AGE

Strictly speaking, it cannot be said that there are any diseases special to length of days, for premature senility shows the changes and diseases usually correlated with ordinary old age. Inherent want of vitality and the resulting degenerative atrophy, or Gowers's abiotrophy, may imitate the results of prolonged wear and tear of the tissues, and thus it appears that Charcot's [1] group of diseases special to old age, namely senile marasmus, senile osteomalacia, senile atrophy of the brain, senile heart weakness, and arteriosclerosis, are not confined to senescence. Old age, however, is prone to the incidence of diseases which are chiefly but not exclusively seen in the evening of life, such as those due to the degenerative changes resulting from the accumulated effect

[1] Charcot, J. M., *Clinical Lectures on Senile and Chronic Diseases*, New Sydenham Society, 1881, p. 33.

of past infections and from metabolic disturbance. Thus arteriosclerosis, granular kidney, cardiac failure, cerebral haemorrhage, emphysema, hepatic cirrhosis, prostatic enlargement, and carcinoma commonly appear in the sixth decade. In a series of five publications dealing with the diseases of the age of fifty, which he calls the critical age, Leclercq [1] describes, in addition to some of the above, gout and paragouty affections, obesity, diabetes, cardio-aortic diseases, and albuminuria. Old age, moreover, modifies the manifestations and course of infections, notably of pneumonia and erysipelas. It would be unnecessary and from reasons of space impossible to refer to all the diseases that may attack the aged, but a few remarks will be made about some disorders that appear to call for special notice.

Senescence has some nosological compensations ; thus some acute infections, such as measles, scarlet fever, enteric fever, and diphtheria, are very rare, probably because immunity has gradually been developed in the course of time ; pneumonia and erysipelas, however, are notable exceptions in being specially prone to occur in the aged. Migraine usually becomes less troublesome or disappears

[1] Leclercq, A., *Les maladies de la cinquantaine*, 5 vols., 1922, Paris.

with the march of years. As mentioned on p. 86, malignant disease is comparatively rare in very advanced age ; lymphadenoma and leukaemia are rarer than in early life ; and as pathological, like normal, processes are slower, carcinoma, especially of the breast, may become stationary.

Diseases of the Skin.—From atrophy of the skin and its secretory glands the skin is less resistant to infection and accordingly has been thought to be more susceptible to parasitic attack, such as pityriasis versicolor. The aged who are often less scrupulous in cleanliness than their juniors are more prone to skin affections, such as eczema, erythema, and erysipelas. The so-called senile prurigo is largely due to the presence of lice. From the atrophic condition of the skin the cutaneous nerves are more exposed, and this has been regarded as playing a causal part in senile pruritus, which is an exception to the general rule that sensory impressions are less prominent in the aged than earlier in life. It may, like prurigo, be due to an external cause, such as pediculi, or it may be metabolic in origin. In almshouses and institutions for the aged epidemics of scratching may develop from imitation of a genuine case of pruritus. Senile

pruritus is usually general and from its obstinate resistance to treatment may be a terrible affliction. Sir Gilbert Blane (1749–1834) suffered from it for the last 13 years of his life, and was obliged to take opium in increasing quantities until his daily dose reached the equivalent of a dram of the solid drug.

Erysipelas, like pneumonia, with which or with bronchopneumonia it may be combined, is less obvious in its symptoms than in ordinary adult life on account of the diminished power of reaction, as shown by the slight degree of leucocytosis in the aged in erysipelas (Lamy) and by its longer course. From want of resistance and arteriosclerosis, especially Mönckeberg's form with calcification of the media, senile gangrene may follow slight accident or injury, such as occurs in cutting the toe nails. Absorption from the gangrenous area may cause toxic glycosuria, and such cases, when they come under observation at this stage, are sometimes regarded as diabetic gangrene. It is remarkable how well amputations for diabetic gangrene do ; in July 1922 I saw with Professor F. H. Edgeworth a man with double amputation of the legs perfectly healed, and in good health though the glycosuria persisted.

Herpes zoster, though far from confined

to advanced life, has in the old the unfortunate tendency to leave persistent pain in its site. Rodent ulcer, although sometimes seen comparatively early in life, is specially common in advanced years. It often supervenes on the dry yellow or brown spots (senile keratosis) seen on the face in persons over 60 years of age.

Vertigo is extremely common in later life and may be due to various causes ; the most frequent form is that of aural origin, such as labyrinthine or nerve lesions and chronic changes in the middle ear. Increased blood pressure and cerebral arteriosclerosis are frequently responsible. Attacks of giddiness may occur in Stokes-Adams disease or follow exertion in the aged, as if from cerebral anaemia ; and gastric disturbance may apparently also be a determining factor. In rare instances epilepsy or migraine may be represented or initiated by vertigo.

Senile tremor, rare under the age of 70, begins in the hands, especially in that most used, and spreads to the neck and head, rarely occurring in the lower limbs. It is a slow intention tremor, from 4 to 5 per second, and is distinguished by its relation to movement from that of paralysis agitans which is continuous but diminished on muscular contraction.

The tremor of the jaw resembles that of munching food ; that of the lips is fine. It is compatible with good health.

Paralysis agitans, described by James Parkinson, surgeon and palaeontologist, in 1817 as " the Shaking Palsy," has now about a century later been shown, largely as a result of S. A. K. Wilson's work, to be one of the forms of the extra-pyramidal symptom complex and due to degenerative changes in the efferent motor system of the globus pallidus system. Although juvenile forms occur and encephalitis lethargica may show the Parkinsonian syndrome, paralysis agitans is a disease of the early part of the later period of life, the great majority of the cases beginning between 50 and 70 (Gowers [1]), after which there is a small incidence only. It is twice as common in males as in females. Though unfortunately, from the degenerative nature of the lesion, incurable, it is a chronic disease ; thus Maclachlan [2] refers to a Chelsea pensioner aged 107 years in whom it was known to have existed for 47 years.

Vascular lesions, haemorrhage or thrombosis, are the most important factors in the production

[1] Gowers, W. R., *System of Medicine* (Allbutt and Rolleston), 1910, viii. 473, London.

[2] Maclachlan, D., *A Practical Treatise on the Diseases and Infirmities of Advanced Life*, p. 213, London, 1868.

of grave nervous disease between the ages of 50 and 70; among 500 cases of cerebral haemorrhage 321, or 64 per cent, and of 110 cases of cerebral thrombosis 67, or 61 per cent, occurred in the sixth and seventh decades (Michell Clarke[1]). *Cerebral haemorrhage* increases with frequency from the fourth decade and the largest number of cases occur between 50 and 60. From analysis of 154 cases at St. Bartholomew's Hospital F. W. Andrewes[2] found that the apparent maximum is in the middle of the sixth decade, but that correction for the age distribution of the population shows that the liability of the individual to this form of death increases steadily up to old age. *Thrombosis of atheromatous vessels* is an accident of later incidence than cerebral haemorrhage, and thus contrasts with hemiplegia due to syphilitic endarteritis which occurs about the prime of life.

The physiological involution of the mind and accompanying organic changes in the brain gradually shade off into senile dementia. A regression to the mental state of childhood, which Dupré[3] called puerilism, may occur in

[1] Clarke, J. M., *Brit. Med. Journ.*, 1915, ii. 665.
[2] Andrewes, F. W., *St. Barth. Hosp. Rep.*, London, 1912, xlviii. 9.
[3] Dupré, E., *Nouv. iconograph. Salpêt.*, Paris, 1905, xviii. 88.

widely different conditions, such as structural change of the brain, hysteria, and toxaemia. It may be acute and be transient or come on slowly and be permanent. Just as an old man may relapse into the speech and accent of his youth, so if he had a hard pecuniary struggle in his early days may he become miserly in the evening of his life.

Senile dementia is an exaggeration of the mental changes occurring in old age and due to further changes in the brain from vascular disease or toxic influences. It varies much in its features ; some patients are maniacal, others depressed and melancholic, some feeble, some delusional, and a few immoral. The senile mania may be mainly nocturnal and was compared by Clouston [1] to the night delirium of a febrile neurotic child ; it may pass into dementia. Of the melancholic group in which suicide may occur Clouston found that 30 per cent recovered.

Senile paraplegia may be divided into four etiological groups : (1) The functional dysbasias or pseudo-paraplegias described by Marie and Léri,[2] which in general terms resemble

[1] Clouston, T., *System of Medicine* (Allbutt and Rolleston), London, 1910, viii. 935.

[2] Marie, P., et Léri, *Séméiologie nerveuse*, *Traité de médecine* (Gilbert et Thoinot), p. 450.

those met with during adult life, but the varieties are less distinct in the old. Quesnel [1] recognizes three groups of functional disturbance of walking in old people : (*a*) the slight and usually curable, (*b*) severe functional disturbance depending essentially on the mental state of the patient, and (*c*) the organo-functional in which a bony, articular, or nervous lesion is present ; thus confinement to bed for a fracture may cause a functional paraplegia. (2) Spastic paraplegia due to sclerosis in the lateral and posterior columns of the spinal cord ; the influence of arteriosclerosis, as advocated by Oppenheim, has been the subject of some debate, and Lejonne and Lhermitte point out that the nervous lesions are not necessarily perivascular and that there is a want of proportion between the vascular and the nervous changes. (3) Paraplegia of cerebral origin with descending degeneration in the cord and mental deterioration. (4) Paraplegia from muscular fibrosis and contracture, the central nervous system being intact.

From the presence of emphysema bronchitis is prone to occur in the old. *Lobar pneumonia and bronchopneumonia.* Lobar pneumonia has always been considered the great enemy of

[1] Quesnel, M., *Thèse de Paris*, 1920, No. 258.

the aged ; it is often latent, and may be found after sudden death and in persons supposed to have died of old age, because they were walking about or complained not at all or only of trivial symptoms. In spite of Charcot's[1] considered opinion to the contrary, it is probable that pneumonia has been often used to describe what was really bronchopneumonia. For Roussy and Leroux[2] found that among 300 necropsies at the Hospice Paul Brousse there were 164 cases, or 55 per cent, of bronchopneumonia and only 4 cases, or 1·4 per cent, of lobar pneumonia. The bronchopneumonic areas are triangular with the base towards the pleural surface, and indeed are infarcts, due to pre-existing endarteritis obliterans which disposes to secondary infection. In 110 out of the 164 cases of bronchopneumonia there was arterial thrombosis, which was of older date than the infected areas of infarction and bronchopneumonia.

Senile tuberculosis, contrary to what has sometimes been stated, is fairly common though it is often latent; a patient with pulmonary tuberculosis may have little or no cough, expectoration, fever, or night sweats, and the physical

[1] Charcot, J. M., *Clinical Lectures on Senile and Chronic Diseases*, New Sydenham Society, 1881, p. 239.

[2] Roussy, G., et Leroux, R., *Ann. de méd.*, Paris, 1921, ix. 161.

signs, if present, may be regarded as those of bronchitis and emphysema or bronchiectasis, unless the sputum is available and examined for bacilli. Such unrecognized cases are an obvious danger in institutions, and it may be added that hereditary disposition plays a much less important part in the aged than in early life. Senile tuberculosis, however, is usually either a persistence of that infection or a recrudescence of quiescent infection, and is seldom primary. The disease may be chronic or acute, and either local or generalized.

The *senile heart* has attracted much attention, and myocardial degeneration and fibrosis due to past infections or to coronary arteriosclerosis are extremely common. The myocardial change is of great importance in reducing the reserve power of the heart, so that cardiac failure is prone to supervene in acute infections, such as influenzal pneumonia. Chronic valvulitis akin to and associated with arteriosclerosis is common ; the mitral valve is often affected and incompetent, with a loud systolic murmur at the apex which is displaced outwards; but the most characteristic lesion of advanced years is pure aortic stenosis ; this is commonly regarded as part of the arteriosclerotic process in the aorta, but, as I have often noticed, the

aorta may be remarkably healthy and even thinner than usual in old people with extensive calcification of the valves reducing the aortic orifice to a chink ; it has indeed been thought that such stenosis of the aortic valves may protect the aorta from strain and so from arteriosclerosis. Although involvement of the bundle of His giving rise to the symptom complex of Stokes-Adams disease, and angina pectoris may complicate aortic stenosis, the presence of this valvular defect is compatible with remarkable prolongation of life. This may be due to the more placid life of these old patients, as is suggested by Sir Clifford Allbutt,[1] who regards aortic stenosis as more unfavourable in persons under 55 years of age than in their elders.

Aneurysm of the large arteries is rare in the aged, although arteriosclerosis is common. Diffuse dilatation especially of the arch of the aorta and of the common iliacs is not infrequent, and occasionally latent saccular aneurysms are present. In rare instances large abdominal aneurysms causing pain or remaining latent until rupture occurs are reported. Among 112 abdominal aneurysms collected by Nunne-

[1] Allbutt, Clifford, *System of Medicine* (Allbutt and Rolleston) London, 1909, vi. 455.

ley[1] 15 were over 50 years of age ; these figures included 32 from St. George's Hospital, three of them being over 65 years of age. Miliary aneurysms are of course extremely common in the subjects of cerebral haemorrhage.

Spasm, especially of arteriosclerotic vessels, may be responsible for attacks of giddiness or faintness, particularly on exertion, and there may be some doubt whether such symptoms are the outcome of cerebral anaemia or of cardiac insufficiency. Frequent transient attacks of aphasia or paralysis, due to spasm of arteriosclerotic middle cerebral arteries, may occur in patients with high blood pressure (Peabody,[2] Osler [3]).

Varicosity either localized, like aneurysms, or throughout the length of veins, are common, especially in the lower limbs of women who have borne children and done much standing ; this condition disposes to varicose ulcers in the lower third of the leg, and to acute phlebitis. As pointed out by Trousseau, who was an illustration of his own dictum, venous thrombosis may occur in the course of intra-abdominal malignant disease.

[1] Nunneley, F. P., *Aneurysm of the Abdominal Aorta*, p. 8, London, 1906.

[2] Peabody, *Trans. Assoc. Amer. Phys.*, Washington, 1891, vi. 170.

[3] Osler, W., *Journ. Canad. Med. Assoc.*, 1911, N.S. i. 919.

Though *dyspepsia* of adult life often diminishes or passes away in the more tranquil conditions of old age, it is common; Fenwick[1] estimated that it occurred in 21 per cent of the population over the age of 65. Oral sepsis may be responsible for chronic gastritis and much debility in the old. *Constipation* often comes on after 60 and is mainly due to atonic dilatation and failure of peristalsis in the colon, though diminished secretion of mucus may play a part. Prostatic enlargement has been thought to interfere with peristalsis (Hollis[2]), and in women large fibromyomas of the uterus may have this effect. Gerontal constipation is usually more troublesome in women than in men. Faecal accumulation in the rectum is a frequent cause, especially in bed-ridden subjects, of what they describe as diarrhoea, the real significance of which may be easily overlooked unless digital examination of the rectum is undertaken. The pecten band of fibrous tissue arising in the submucosa of the pecten, inside the external sphincter, narrows the anal orifice and so prevents complete evacuation of the rectum and diminishes the size of the faeces which are generally voided in short pieces. It

[1] Fenwick, W. S., *Lancet*, 1909, ii. 1346.
[2] Hollis, W. A., *Brit. Med. Journ.*, 1916, i. 677.

is usually, but not always, associated with internal piles and due to the attendant congestion. W. E. Miles,[1] who described the pecten band, tells me that it may be regarded as a pathological development of advancing years, and that he has found that it may so reduce the anal orifice in the elderly that it is with difficulty the little finger can be introduced. Pruritus ani, due to piles and local congestion, is not uncommon in the aged.

Piles are common in the aged and are related to the frequency of constipation. Like other diseases, they do not give rise to discomfort so soon or so forcibly as in younger persons. From muscular atrophy hernia, umbilical in both sexes, in men inguinal and in women femoral, is prone to occur.

Gallstones are more frequent in advanced life, especially in women, than at other times of life, gallstones being found after death in about a third of persons over 70 years of age, though, as mentioned elsewhere, biliary colic is comparatively rare in old age.

The *urinary bladder* in cases of prostatic enlargement shows hypertrophy succeeded by dilatation, fasciculation, and sacculation in response to the obstruction to micturition and

[1] Miles, W. E., *Surg., Gyn., and Obstet.*, 1919, xix. 497.

degeneration of the muscular fibres. The ureters in similar circumstances become dilated, and the incidence of cystitis and pyelonephritis is thus favoured.

Arthritic Affections.—Although gout is due to a defect in protein metabolism analogous to diabetes mellitus as regards carbohydrate metabolism and to obesity as a manifestation of disordered metabolism of fat, reference to this disease may be made here. Heredity has a potent influence on the incidence of the disease particularly in early life, but acquired gout is essentially a disease of the latter part of life or the early stage of old age when degeneration is beginning. The first attack may not occur until old age, and is then usually mild in character, and, in Sir William Roberts's [1] words, appears almost as if it were an incidence of senescence. How far the various conditions spoken of as irregular gout, goutiness, or paragouty diseases, which are so numerous as to recall Murchison's lithaemia, should be regarded as gouty is uncertain, but that they depend on disordered protein metabolism is highly probable. The connexion of gout with infection, as urged by Llewellyn,[2] has a bearing

[1] Roberts, W., *System of Medicine* (Allbutt and Rolleston), 1907, iii. 124, London.

[2] Llewellyn, L. J., *Gout*, 1920, London.

on the fibrositis and Dupuytren's contraction often regarded as gouty phenomena. Dupuytren's contraction of the palmar fascia, which has been thought in some instances to be secondary to arteriosclerosis of the medulla oblongata (Jardini [1]), often accompanies the fibrous pads on the interphalangeal joints of the fingers described by Garrod [2] and Hale-White.[3] The tendency of focal infections, especially oral sepsis, to become more frequent with advancing years also has a distinct bearing on the occurrence of chronic infective arthritis of various forms. The most characteristic is morbus coxae senilis which is not uncommonly associated with Heberden's nodi digitorum, and sometimes with Morrant Baker's cysts due to distension of synovial bursae with fluid ; it may be confused with sciatica. Heberden's nodes are unimportant and commonly free from attendant symptoms.

Spondylitis deformans with ankylosis of the articulations and ossification of the ligaments of the spine, in some cases further complicated by an extension of the process to the proximal joints of the limbs (rhizomelic spondylitis), may occur in the aged though also earlier in life.

[1] Jardini, *Nouv. iconograph. Salpêtr.*, Paris, 1906, xix. 553.
[2] Garrod, A. E., *Brit. Med. Journ.*, 1904, ii. 8.
[3] Hale White, W., *Quart. Journ. Med.*, Oxford, 1907–1908, i. 47.

Osteitis deformans or Paget's disease of bone begins as a rule in the later half of life, the average age being 50 years. Lannelonge[1] and Fournier[2] argued that it is a lesion due to congenital syphilis ; but although luetic periostitis and osteitis may imitate it, there is no convincing evidence in favour of their contention.

[1] Lannelonge, *Bull. Acad. de méd.*, Paris, 1903, 3e sér., xlix. 299.
[2] Fournier, *Ibid.*, 1903, 3e sér., xlix. 522.

INDEX

Abernethy, J., 84
Abiotrophy, 139
Acquired characters, 35, 75, 79
Activity. *See* Functional; Muscular
Adam, age of, 14
Adami, J. G., 87
Adolescence, termination of period of, 17
Adrenals, 110
Age, the "critical," 140
  the "dangerous," 26
  exaggeration of, by elderly people, 20, 21
Albuminuria, 126
Alcohol, abuse of, 57
  action of, on the tissues, 57
  influence on longevity, 33, 34, 57
Alimentary canal, lymphoid atrophy of, 109
Allbutt, Clifford, 37, 55, 59, 150
Allen treatment of diabetes, 56
Amputation, for diabetic gangrene, 142
Anabolism, cellular, 67
Anaemia, secondary, 108
Anal orifice, narrowing of, 152
Anatomical changes, 60, 63, 90-114
Andrewes, F. W., 145
Aneurysms, 150, 151
Angiomas, 108
Animal life, duration of, 17, 18
  experimental modification of life cycle and growth of, 11
  natural death in, 13, 14
  rejuvenation and senescence in, 9-11
Aortic stenosis, 149
Aphasia, transient attacks of, 151
Appetite, 56, 118
Arcus senilis, 98
Arnold, M., 123
Aron, 75
Arteries, degenerative changes in, 97, 105-107
  "pipe-stem," 106
Arteriosclerosis, 97, 105-107, 149
  age incidence of, 105, 140
  causes of, 105, 142
  hereditary transmission of, 37
  influence of smoking on, 59
  prostatic hypertrophy and, 112
  spasm associated with, 151
  thyroid prevention of, 73
Arthritic affections, 154
Arthritis, chronic infective, 155
Atheroma. *See* Arteriosclerosis
Athyroidism, 73
Atkinson, Edward, nonagenarian, 51
Atrophy—
  brown, 103, 105
  cardiac, 104, 140, 149
  degenerative, 46
  general, 62, 91, 139
    causes of, 137, 138

Atrophy (*contd.*)—
genital, 114
lymphoid, 108
muscular, 103
of auditory nerve, 118
of skin and secretory glands, 141
of thymus, 109
precocious, 138
renal, 111
splenic, 109
testicular, 113
Atropine, 127, 128
Aub and Dubois, 116
Auditory nerve, atrophy of, 118
Auto-suggestion, 48

Bacon, Francis, 17, 95
Bacon, Roger, 17
Baddeley, J. J., 51
Baldness, 95
causes of, 96
thyroid extract in, 96
Barclay-Smith, E., 82
Baronsdale, W., 5
Bell, B., 75
Bell, J. R., 115
Benjamin, H., 77
Berman, L., 71
Biedl, A., 71
Biochemistry of old age, 64-68
Biological aspect of old age, 10, 11, 23, 63
Biotripsy, 93
Birth, expectation of life at, 13, 41, 42
Birth control, 24
Bladder, 133, 153
Blane, G., 142
Blood, condition of, 108, 115
increase of urea-nitrogen in, 115
Blood pressure, 125
and heredity, 37
high, 55, 124
longevity in relation to, 37
senile, 104, 124, 125
Blood supply, diminished, 106
Blood transfusion, 66
Bodily vigour, sex gland activity as manifestation of, 69
Body, cells of. *See* Cells
conformation of, 60
fibrous framework of, 92
structural changes in, 90
temperature of, 116
water content at birth and adult life, 64
Boerhaave, 91
Bone marrow, atrophy of, 108
Bones, injuries to, healing of, 126, 127
Paget's disease of, 156
rarefaction and absorption of, 99
arterial degeneration with, 107
Bony changes, 98, 99
Bouin and Ancel, 73
Brain, changes in, 96, 146
degeneration of cells of, 97
organic changes in, 145
senile atrophy of, 139
shrinkage of, 100
weight of, 97
Brain cells, activity of, influence on longevity, 35, 36
Brampton, Lord, nonagenarian, 51
Bromides, intolerance to, 128
Bronchiectasis, simulating tuberculosis, 149
Bronchitis, disposition to, 147
simulating tuberculosis, 149
Bronchopneumonia, 148
and pneumonia, confusion between, 148
tendency to, 103
Brown atrophy, 103, 105
Brown-Séquard, 70
Browne, T., 14, 47, 95
Brownlee, J., 33
Buffon, 17
Butler, Samuel, 35

Calcification, of arteries, 106-107
of cartilage, 100
Calendar, length of, in the patriarchal era, 15
California, centenarians in, 41
Cambridge University, influence of John Haviland on the study of medicine, 6

Cameron, C., 95
Campbell, H., 65
Cancer. *See* Carcinoma
Carcinoma, 141
  age and sex incidence of, 86, 140
  and senescence, 86-89
  rarity of, in extreme old age, 87
Cardio-vascular system, 36-38, 103-108, 124, 133, 149
Carlisle, Anthony, 8
Carrel, A., 65, 66, 127
Cartilages, calcification of, 100
Castration, phenomena of old age and, 79
  secondary sex characters following, 79
Cazalis, 107
Cell-memory, 35
  longevity in relation to, 35
Cells, 62
  activity of, relation to connective tissues, 68, 88, 89, 92
  ageing of, 67, 88
    carcinoma in relation to, 86-89
    causes and significance of, 67
    senility in relation to, 86, 88
  changes in, infections causing, 43, 44
  changes in old age, 64
  colloidal changes in, 64, 68
  cultivation of, 66
  degeneration of, 62, 92, 135
    intestinal bacteria causing, 82, 83
  infections and intoxications producing changes in, 44
  life cycle of, 63, 65, 88, 89
    factors influencing, 65
    on what dependent, 68
    thyroid deficiency influencing, 72
  limited vitality of, 62
    sequels of, 64
  products inimical to life of, 65
  senile changes due to injury to, 30, 31, 67
  time-rate of, 36
  vital phenomena of, 63, 88, 89
Census returns, 41, 43
Centenarianism, 19
  heredity in relation to, 19
Centenarians, 20, 33, 34
  age exaggeration by, 20, 21
  among Churchmen, 50
  among doctors, 52
  among professional men, 50
  census returns of, 20, 21
  family incidence of, 32, 33
  in California, statistics, 41
  in England and Wales, statistics, 40, 41
  in Ireland, statistics, 40
  medical, 52
  personal habits of, 56, 57
  rarity of cancer among, 87
  sex statistics of, 21, 22
  smoking among, 58
  statistics of, 21, 24
    deaths among, 21, 22, 41
Cerebral arteries, changes in, 97
Cerebral degeneration, 97
Cerebral haemorrhage, 145
  age incidence of, 145
Cerebral thrombosis, 145
Chaderton, Laurence, centenarian, 51
Charcot, J. M., 8, 104, 116, 139, 148
Cheatle, G. L., 93
Chest capacity, diminished, 103
Cheyne, G., 55
Child, C. M., 10, 14, 56
" Childhood, second," 122, 145
Chromophages, 94
Chromosomes, 88
Churchmen, centenarians among, 50
Cicero, 135
Circulatory system, 38
Clark, Andrew, 29, 60, 137
Clarke, E., 85, 98
Clarke, J. M., 145
Climacteric, ancient conceptions of, 27
  senile, 30
Climacteric disease, 28
Climate, influence on longevity, 26, 39
Coke, Sir Edward, octogenarian, 51

Colloidal dehydration, leading to old age, 64, 65
Colon, destruction of putrefactive bacteria in, 83
Constipation, 101, 152
  age incidence of, 152
  gerontal, 102
  tendency to, 115
Cornaro, on the duration of life, 18
  writer on old age, 8
Costal cartilage, calcification of, 100
Councilman, W. T., 37, 92, 104, 107, 111, 125
Cranial bones, changes in, 100
Crosby, T., 51
Cushny, A. R., 81
Cutaneous sensation, 117
Cystitis, 154

Darwin, C., 53
Deafness, causes of, 118
  senile, 118
Death, causes of, 13, 38
  mental attitude to, 123
  natural, 13, 14, 16, 91
    from old age, 14, 91
    in animal kingdom, 13, 14
    probable cause of, 36
    Weissmann's conception of, 9, 16
  phenomenon of, 9, 10
  sudden, causes of, 117
    latent pneumonia causing, 148
Death-rate, in various countries, 42
  sex incidence, 22
Deaths, among centenarians, 41
Decrepitude, 30
Delirium, 146
Delusions, 146
Demange, 91, 105
Dementia, senile, causes of, 146
  onset of, 145
  varied features of, 146
" de Morgan's Spots," 108
Dental decay, 101
  an accompaniment of old age, 44, 45
Dentition, third, explanation of, 101
Depression, senile, 146
de Salis, Cardinal, centenarian, 50
Descartes, 7
Desmond, Countess of, centenarian, 20
Devolution, course of, 122
Diabetic gangrene, 142
Diet, restricted, influence of, 56
Digestion, impairment of, 101
Digestive system, 38
Disabilities of old age, 90-114, 137
Disease, associated with old age, 30, 44, 139
  chronic, freedom from, in old age, 44
  definition of, 136
  influence of, on longevity, 43
  latency of, 117
  old age as a, 49, 136
Doctors, duration of life of, 52, 53
  centenarian, 52
Donaldson, R., 110
Drew, A., 68
Drinkwater, H., 52
Drugs, reaction to, 127-128
  reaction to, during senescence, 127
Dryness of elderly bodies, 64
Ductus cochleariæ, fibrosis of, 118
Dupuytren's contraction, 155
Dysbasia, functional, 146
Dyspepsia, frequency of, 152

Early rising, 59, 60
Ears, disorders of, 143
Easton, J., 20, 47
Ebstein, 18
Eccentricities of old age, 120, 121
Ecclesiastes, interpretation of, 129
Eczema, 118, 141
Emphysema, 147, 149
Endarteritis obliterans, 103
Endocrine glands, in relation to old age, 12, 68-81
Endomixis, 9
Environment, influence on longevity, 33, 34, 39-46, 55
Erysipelas, 141
  disposition to, 140
  senile, course of, 142

Erythema, 141
Eunuchs, duration of life of, 79
Expectation of life, 13, 41
in various countries, 42
Extra-systoles, 124
Eyes, senile disorders of, 117

Facial appearance, 93
changes in, 93
causes of, 118
Fads, 121
Faintness, 151
Fat, reduction of, 92
subcutaneous, disappearance of, 94
Fatigue, excessive, danger of, 54
physical and mental, 119, 120
psychical, 122
Fatty degeneration of arteries, 106
of heart, 104
of muscles, 103
Femur, fracture of, 99, 127
Fertility, age limit of, in women, 26
average, estimation of, 24
old age in relation to, 23, 24, 26
social conditions influencing, 24
Fibrosis, 91, 92
Fibrositis, 155
Fibrous tissues, atrophy of, 91
Finot, J., 49
First-born, handicapping of, 38
longevity in relation to, 38
Flourens, on the duration of life, 18
Food, excess of, 56
Fractures, delay in healing of, 126, 127
tendency to, 99
France, longevity in, 40
Functional activity, danger of excess of, 54
influencing longevity, 46, 55
progressive diminution in, 115, 119, 135

Gait, disordered, 122, 147
Galileo, 53
Gallstones, 153
Gangrene, diabetic, 142
senile, 142
pipe-stem arteries with, 106
Garrod, A. E., 155
Gastric juice, composition, changes in, 115
lack of, 101
Gastro-intestinal tract, changes in, 101
Generation. *See* Reproductive power
Generative organs, internal secretion of, 70, 73-80
Genitals, external, atrophy of, 114
Giantism, 19, 20
Giddiness, 143
causes of, 151
Gilford, H., 30, 72, 88
Gisborne, Thomas, Linacre lecturer, 5
Gland activity, functional, diminution of, 115
senility in relation to, 69
Gland atrophy, 109, 110
Gland cells, life cycle of, 67
Gland secretions, influencing activity of body-cells, 68, 69
Gland, endocrine, metabolism stimulated by, 81
rejuvenescence in, in relation to, 12, 73-80
Gland, endocrine, theory of old age, 70, 71, 72
Gland, endocrine, therapy during old age, 71
of prostatic enlargement, 113
rejuvenescence in relation to, 12, 73-80
See also Endocrine, Pituitary, etc.
Glycosuria, 126
toxic, cause of, 142
Goethe, 53
Goodpasture, E. W., 88
Gout, 154
acquired, age incidence of, 154
Gowers, W. R., 139, 144
Graves, R. J., 95

Gray, A. A., 118
Greenwood, Major, 24
Gregory IX., centenarian, 50
Growth, 60
  experimental modification of, 11
  influence of endocrine gland therapy on, 12, 72, 80
  retardation by vitamine deficiency, 13

Habits, influencing longevity, 55
Haemoglobin, 108
Haemorrhage, 144
  cerebral, 145
Hair, changes in colour of, 94
  excessive growth of, 96
  of the body, loss of, 96
Hale-White, W., 109, 155
Hall, Bishop, 131
Hall, Stanley, 8, 27
Haller, 91
Halsbury, Lord, nonagenarian, 51
Hands, appearance of, 93
  atrophic changes in, 94
  senile tremor of, 143
Harrower, 80
Haviland, John, influence on the Cambridge medical school, 6
  Regius Professor of Physic, 6
  Linacre lecturer, 5
Head, senile tremor of, 143
Health, definition of, 136
Hearing, impairment of, 118
Heart, atrophy of, 104
  condition of, 92, 103, 104
  diseases of, 149
  failure, 149
    age incidence of, 140
  hypertrophy of, 55, 104
    and blood pressure, 104
    longevity in relation to, 37
  senile changes in, 104, 139, 149
Heberden, W. (the elder), 4, 54
Heberden's nodes, 155
Height, cause of loss of, 100
Hereditary tendencies, correction of, 34
Heredity, firstlings in relation to, 38
  influence on longevity, 19, 32-39
Hernia, tendency to, 153
Herpes zoster, 142
Hertoghe, 113
Hetero-suggestion, 48
High altitudes, influence on longevity, 39
Hippocrates, age of, 52
Holland, Henry, 28
Holmes, O. W., 49
Hopkins, G., 13
Hot climates, influence of, on senescence, 26, 36, 39
Huchard, 59, 105
Hufeland, C. W., 17, 23, 70
Humphry, G. M., 8, 22, 32, 34, 39, 43, 58, 60, 87, 98-100, 112, 124
Hunter, W., 124
Huxley, J. S., 11
Hygiene of old age, 55-61
Hyperpiesia, 37, 124
Hypertrichosis, following the menopause, 96
Hypnotics, 128
Hypochondriasis, 121
Hypoplasia, 63, 64
Hypothyroidism, in relation to old age, 72

Idleness, inimical to old age, 46, 47
Individuation, phenomenon of, 10
Infant mortality, sex incidence and causes, 22
Infantilism, premature senility with, 31
Infections, 140
  cell changes due to, 43, 44
  disposition to cardiac failure during, 149
  focal, tendency to, 155
  gout in relation to, 154
Insomnia, 119
Interstitial cells, 73-81
Intestinal stasis, as cause of premature old age, 82, 85

Intoxications, cause of senescence, 82
influence on body cells, 44, 55
Invalidism, auto- and hetero-suggestion producing, 48
Ireland, centenarians in, 40
Iris, sluggish, 117
Iverex, Dr., centenarian, 32

Jackson, Christopher, 3
Jackson, Hughlings, 122
James, R. R., 52
Jastrow, M., 130
Jaw, changes in shape of, 99
tremor of, 144
Jenkins, Henry, centenarian, 20
Jews, longevity of, 40
Johnson, S., 46
Joints, fractures of, disposition to, 99

Keratosis, senile, 143
Kidneys, 126
degenerative changes in, 111
granular, age incidence of, 140
King, G., 20
Klotz, O., 107
Knee-jerk, 119
Koheleth, 139
Kuntz, A., 74

Labyrinthine deafness, 118
Labyrinthine vertigo, 143
Lacassagne, A., 30, 55
Lane, W. Arbuthnot, 84
Lankester, E. Ray, 14, 19, 23
Laryngeal cartilage, calcification of, 100
Laurent, O., 41, 87
Laurentius, Andreas, 29, 46, 116, 131
Lazarus, 59
Lazarus-Barlow, W. S., 86
Leclercq, A., 140
Léri, 83, 146
Leroux, 103, 148
Lessius, Leonardus, 55
Leucocyte count, 108, 109
Leucodermia, 93
Leukaemia, 141
Leydig, interstitial cells of, 73-81
Lichtenstern, 77
Life, animal and human, duration of, 17, 18
chronometry of, 138
climacterics of, 27, 30
duration of, 9
among professional men, 50-53
chemical theory of, 66
early theories of, 17
estimation of, 18
in vitro, 66
various writers on, 17, 18
variation in different countries, 39
modern theories of, 18
expectation of, at birth, 13, 41
prolongation of, experimental, 12, 13, 77
following cessation of reproductive function, 23
See also Longevity
Life cycle, experimental modification of, 11
Ligament, spinous, ossification of, 99
Ligamentum spirale, atrophy of, 118
Linacre, Thomas, 2
family history of, 2, 3
Linacre Lectures, 3-6
Linacre Lectureship, 1
Lips, tremor of, 144
Lipschülz, 74
Liveing, G. D., 7
Liver, atrophy of lobules and cells of, 102
changes in size and weight of, 102
cirrhosis of, 140
Llewellyn, L. J., 154
Longevity, alcohol influencing, 57
among professional men, 50, 53
auto- and hetero-suggestion influencing, 48, 49
"cell-memory" in relation to, 35
climatic conditions influencing, 39, 41
conditions favouring, 7, 33

Longevity (*contd.*)—
diseases inimical to, 45
endocrine atrophy in relation to, 68-81
environment influencing, 33, 34, 39-46, 55
factors influencing, 32
fertility in relation to, 23, 24
functional activity influencing, 46, 55
hereditary aspects of, 19, 32-39
idleness inimical to, 47, 48
in the medical profession, 52
influence of past diseases on, 43
influence of blood pressure on, 37
influence of brain cells on, 36
integrity of cardio-vascular system necessary to, 36
of nations, compared, 39, 40
of the patriarchs, 15, 16
personal habits influencing, 55
potential, on what determined, 67
sex incidence of, 21, 22
smoking in relation to, 58
syphilis preventing, 45
vitality of central nervous system essential to, 36
See also Old Age ; Senescence
Lorand, A., 70
Lowe, Peter, 131
Luciani, 18, 102
Lungs, changes in, 103
diseases of, 147, 148
Lydston, G., F., 71
Lymphadenoma, 141
Lymphoid tissues, atrophy of, 63, 108

Maclachlan, D., 144
Maignon, Abbé, centenarian, 50
Malignant disease, 87, 141
cell senility in relation to, 88
Mammae, involution changes in, 114
Mania, senile, 145, 146
Mansell-Moullin, C. W., 78
Mansfield, Lord, octogenarian, 51
Marasmus, senile, 139
Marie, P., 146
Marinesco, 64, 78, 83, 97
Marx, K., 47
Mead, Richard, 131
Medical men, centenarians among, 52
duration of life of, 52, 53
Melancholia, senile, 146
Memory, impairment and loss of, 120, 122
Menopause, onset of old age at the, 26
ovarian changes at, 63, 79
Mental activity, influence on old age, 47, 48, 50, 54
unimpaired, in advanced age, examples of, 50, 51, 53
Mental deterioration, 49, 119, 122, 145, 146
causes of, 47, 48, 49
onset of, 53
Mental fatigue, tendency to, 120
Mental state, 119, 122, 123
and the physical, want of harmony between, 123
influence of, 48-50
Metabolism, disordered, 115, 116, 117, 154
gland therapy stimulating, 72, 81
Metchnikoff, E., 8, 13, 18, 82-86, 91, 97, 123
Methuselah, 14
Michael Angelo, mental activity at advanced age, 53
Micturition, disorders of, 153
Middle ear lesions, 143
Migraine, 140
Miles, W. E., 153
Mind, 121
and body, in old age, 47, 50
disintegration of, 120
disorders of, 122, 145, 146
See also Mental
Molière, 53
Mönckeberg's sclerosis, 106
causes of, 142
Montaigne, 14, 56
Moon, R. O., 136
Moore, Norman, 5

Morbus coxae senilis, 155
Morphine, 127, 128
Mott, F. W., on functions of cells of testes and ovaries, 75
Muscles, voluntary, changes in, 103
Muscular activity, danger of excess of, 54
impaired, 99, 119, 135
Muscular atrophy, 99, 119, 135
among workmen, 54
Myocardium, degeneration of, 104, 149
Myxoedema, as secondary senilism, 72

Nails, condition and appearance of, 96
Nanism, senile type of, 31
Nascher, I. L., 30, 98, 127
Nathan, 68, 74
National habits, influence on longevity, 40
Natural death. *See* Death
Neck, senile tremor of, 143
Nemenow, 112
Nephropathy, chronic atrophic, 111
Nerves, cutaneous exposure of, 141
Nervous apprehension, tendency to, 122
Nervous disease, 145
Nervous system, 38
vitality of, hereditary factor in longevity, 36
Neurasthenia, 122
New growths, rarity of, 87, 89
Newton, Isaac, 53
Nicotine, effects of, 59
Nunneley, F. P., 151

Obesity, 60
Occupational neuroses, 54
Octogenarians, among active professional men, 51
census statistics of, 21
Oertel, H., 88
Old age, acceleration of, factors favouring, 26
Old age (*contd.*)—
anatomical and physiological changes in, 63
as a disease, 47, 136
attainment of, on what dependent, 6, 7, 10
biochemistry of, 64-68
biological aspect of, 10, 11, 23
bodily conformation in, 60
causes of, 62-89
cell changes leading to, 64, 65
" cell-memory " in relation to, 35
comparative freedom from chronic disease in, 44
death during, common causes of, 38
disabilities of, 137
disease in relation to, 44
diseases associated with, 93-114, 139-156
fertility rate in relation to, 23, 24, 26
glandular, endocrine, theory of, 70, 71, 81
healthy and morbid, distinction between, 135
hereditary aspects of, 32-39
hygiene of, 55-61
infantilism and, 31
mental activity during, 50, 54
examples of, 50, 51, 53
natural death from, 14
on what dependent, 10
onset of, 26
signs of, 29
pathological, 30, 82, 90
of septuagenarians, 53
physiological, 26, 90, 135
physiological and pathological confusion between, 90
factors in, 26
physiology of, 115
premature, 30
hot climates favouring, 26, 36
intestinal stasis as a cause of, 85
mental causes of, 48, 49

Old age (*contd.*)—
production of, Metchnikoff's theory, 83
rarity of natural death from, 14, 91
sex incidence of, 21, 22
stages of, 29
vitality of body cells in, 62-68
writers on, 8, 15, 16
See also Senescence ; Longevity
Onychogryphosis, 96
Ophülz, W., 105
Oral sepsis, 44, 155
Orthobiosis, 55, 84
Osler, W., 2, 36, 151
Osteitis deformans, 156
Osteomalacia, senile, 139
Osteoporosis, senile, 99
Ovarian extract, rejuvenescence in relation to, 80
Ovaries, activity and function of cells of, 73, 74
degenerative changes in, 114
fibrotic atrophy of, 63
following menopause, 79
in relation to senescence, 75
internal secretion of, evidence of existence of, 79
senile, 114
Over-eating, 56, 118
Overwork, danger of, 54
Owen, I., 57

Paget, James, 36, 138
Paget's disease of bone, 156
Pain, blunting of sensibility to, 117
Pallor, 93
Pancreas, fibrotic atrophy of, 102
Paralysis agitans, 144
age and sex incidence of, 144
causes of, 144
senile tremor compared with, 143
Paraplegia, senile, 138, 146
causes of, 146, 147
varieties of, 147
Parathyroids, 110
Parietal bones, changes in, 100
Parkinsonian syndrome, 144
Parr, Thomas, centenarian, 20
Pathological old age, 53, 82, 90
Patriarchal ages, length of the calendar during, 16
Patriarchs, explanation of reputed old age of, 15, 16
Pearson, K., 38, 86
Pecten band, 152, 153
Penis, changes in, 114
Pennington, Isaac, 6
Peristalsis, failure of, 152
Philalethes, Eugenius, on old age, 15
Phlebitis, 151
Phlebosclerosis, 107
Physical and mental states, want of harmony between, 123
Physiological life of man, 19
Physiological old age, 90
and morbid senility, distinction between, 135-138
Physiology of old age, 115-128
Pigmentation, cellular, 103
cutaneous, 93
Piles, 153
Pitman, Henry, medical centenarian, 52
Pituitary extract, influence on weight and growth, 12
rejuvenescence in relation to, 12, 80
Pityriasis versicolor, 141
Planarian flat worms, experimental modification of life cycle and growth of, 11
Plasma, vital phenomena of, 65-67, 88
Plethora, senile, 124
Pneumonia, 147, 148
disposition to, 140
sudden death from, 117
Premature senility, 30
causes of, 48
hot climates predisposing to, 26, 36
syphilis producing, 45
Presbyopia, 117
Pringle, J. J., 94
Prior, Matthew, 3

Professional men, age of retirement of, 54
longevity of, 50-54
Progeria, 30
Prostate gland, 27
climacterium virile due to changes in, 27
hypertrophy of, 101, 112
age incidence of, 140
cause of, 112
cell changes in, 112, 113
glandular therapy of, 113
vesical disorders due to, 153
senile changes in, 111
Protoplasm, products inimical to vitality of, 65
vital phenomena of, 64, 65, 88
Protozoa, rejuvenation and senescence in, 9-11
Prurigo, senile, 141
Pruritus, senile, 141, 142
Pseudo-paraplegia, 146
Psychical activity, diminished, 119
Psychical fatigue, 122
Puberty, functional activity of cells of testes and ovaries at, 75
period of, 17
" Puberty gland," 73
Puerilism, 122, 145
Pulmonary changes, 103, 147
Pulmonary tuberculosis, 148
Pulse-pressure, 125
Pulse-rate, 124
Pupils, contraction of, 117
Purgatives, 128
Pyelonephritis, 154

Quinquagenarians, diseases of, 140, 145, 156

Rectum, faecal accumulation in, 152
Reflexes, 119
Regression, 122
Rejuvenescence, 10
associated with reproduction, 9, 10, 64
attainment of old age dependent upon, 9, 10
experimental production of, 76, 77
Rejuvenescence (*contd.*)—
following vasectomy, 78
gland extracts in production of, 12, 73, 80, 81
in animal life, 9, 10
power of reproduction favouring, 23, 24, 69
restricted diet in relation to, 56
testicular grafts producing, 77
Renal inadequacy, 126
Reproductive power, favouring rejuvenescence, 23, 24, 69
waning of, onset of old age following, 26
prolongation of life after waning of, 23
Retas, Joseph, centenarian, 33
Rheumatism, in old age, 44
Rhizomelic spondylitis, 155
Rhondda, Lord, 49
Richardson, B. W., on the duration of life, 18
Rivers, W. H. R., 122
Roberts, W., 154
Robertson and Ray, 12, 60
Rodent ulcer, 143
Roussy, G., 103, 148
Routh, Martin, centenarian, 50
Roy, D., 32, 95
Russian peasants, longevity of, 40

Salimbeni and Gery, 63, 84, 93, 102
Sand, K., 75
Saundby, R., 8, 44, 85
Savage, G., 34
Sclerosis, arterial, 105-107
Mönckeberg's, 106, 142
spinal, 97
Scrotum, 114
" Second childhood," 122, 145
Sedatives, 128
Self-preservation, instinct of, 122
Self-reliance, loss of, 48, 49
Seminal tubules, activity and function of, 74
atrophy of, 74, 112, 113
prostatic enlargement following, 112
regeneration of, 74

Senescence, 136
castration not a disposing factor to, 79
causes of, 62-89
Metchnikoff's theory, 82, 83
pathological, 82
toxaemic, 82
cell changes during, 62-68
in ovaries and testes, 75, 76
colloidal dehydration leading to, 64, 65
diseases associated with, 139
endocrine glands in relation to, 68-81
healthy and morbid, distinction between, 135
nosological compensations of, 140
progress of, 135
rarity of carcinoma in, 87
rejuvenescence necessary to, 10
thyroid deficiency in relation to, 72
See also Longevity ; Old age
Senile climacteric, 30
Senile type of nanism, 31
Senility, 136
Senium ex morbo, 136
Sense organs, impairment and failure of, 117-121
Sensibility to pain, blunting of, 117
Septuagenarians, nervous disease among, 145
pathological old age of, 53
Sex characters, secondary, cause of, 75
following castration, 79
Sex glands, changes in, *climacterium virile* due to, 27
internal secretion of, 70
Sex incidence of old age, 21, 22
Sexagenarians, diseases common to, 140
nervous disease among, 145
Sexual activity, as manifestation of bodily vigour, 69, 70
duration of, 69
leading to rejuvenescence, 69
waning of, 126
Sexual appetite, on what dependent, 75
perverted, 114
Sexual atrophy, as cause of old age and senility, 69-71
Shaking palsy, 144
Sharpey-Schafer, E. A., 63
Sight, impairment of, 117
Sinclair, John, 8, 20, 35
Singer, C., 86
Skeleton, changes in, 98
Skin, 93, 115
diseases of, 141
disposition to, 141
dry, 115
venules and angiomas on, 108
Skull, 100
Sleep, diminished, 119
over-indulgence in, 60
Smell, impairment of sense of, 117
Smith, John, 8, 131
Smith, Lapthorn, 53
Smoking, influence on longevity, 58-59
Sophocles, mental activity at advanced age, 53
Sour milk, destruction of intestinal bacteria by, 83
Spasm of arteriosclerotic vessels, 151
Spastic paraplegia, 147
Spinal cord, degenerative changes in, 97, 147
Spleen, atrophy of, 63, 109
Spondylitis, rhizomelic, 155
Spondylitis deformans, 99, 155
Stapes, fixation of, 118
Starvation, influencing the onset of senescence, 56, 57
Starvation treatment, 56, 57
Steinach, E., 11, 77, 78
Sterne, John, on the attainment of old age, 16
Stevenson, T. H. C., 41
Strachey, L., 47
Structural changes of the body, 90
Symmers, D., 102
Syphilis, influence on longevity, 45

Taste, impairment of, 117
Teeth, decay of, 44, 101
loss of, 44, 45, 99, 101
causes of, 101
Temperance, a characteristic of centenarians, 57
Temperature, and longevity, 26
of body, 116
Testes, atrophy of, 113
cells of, activity and function of, 73, 74
in relation to senescence, 75
changes in, following vasectomy, 77, 78
internal secretion of, 69-72, 74
prostatic atrophy in relation to, 112
Testicular extract, rejuvenescence in relation to, 80
Testicular grafts, rejuvenation by, 71, 72, 77
results of experiments, 76, 79
Thompson, R. J. C., 37, 44, 49, 96, 125
Thompson, W. J., 40
Thrombosis, 144
age incidence of, 145
cerebral, 145
venous, 151
Thymus, atrophy of, 109
Thyroid deficiency, 138
baldness resulting from, 96
effect on activity of body cells, 72
prostatic enlargement in relation to, 113
Thyroid extract, rejuvenescence in relation to, 80
for prostatic enlargement, 113
Thyroid gland, degenerative changes in, 109, 110
Tinnitus, 118
Tissues, connective, relation of cellular activity to, 68, 88, 89, 92
Titian, 53
Tobacco, and arteriosclerosis, 59
influence on longevity, 58
symptoms due to, 59
Todd, R. E., 37, 44, 49, 125
Toxaemia, as a cause of senescence, 82, 86
degenerative changes due to, 44, 55, 56, 86
intestinal, as cause of senescence, 82, 85
over-eating causing, 56
Transfusion, 66
Tremor, senile, 143
Tropical life, influence on longevity, 26, 36, 39
Trousseau, 151
Tuberculosis, senile, 148
Tumours, 86, 141
Turnbull, H. M., 106, 114

Ulcer, rodent, 143
Urea-nitrogen in the blood, 115
Urinary bladder, hypertrophy of, 153
Urine, condition of, 126
Uterine changes, 114

Valvulitis, chronic, 149, 150
Vanity, senile, 120, 121
Variation, correlated, 23
Varicosity, 151
Vascular lesions, 144
Vasectomy, changes due to, 74
changes in testes following, 77, 78
effect on sexual activity, 76
rejuvenescence following, 71, 78
Veins, changes in, 108
Venous thrombosis, 151
Vertebrae, changes in shape of, 99
Vertigo, causes of, 143
Visceral degeneration, 102, 103
Visceroptosis, 102
Vitality, danger of excess of, 54
loss of, 115, 119, 135
waning of, 139
Vitamins, influence on growth, 13
Voltaire, mental activity at advanced age, 53
Voronoff, testicular grafting by, 78

Walker, Kenneth, on changes in the testes, 112
on prostatic enlargement, 112, 113
Walking, functional disturbances in, 147
Waterhouse, B., on the onset of old age, 27
Watson, Thomas, Linacre Lecturer, 5
Weber, Hermann, 8, 34, 43, 57, 119
Weber, Parkes, 35, 104
Weissmann, 9, 16
" Will to live," 35, 47
Will power, failure of, 122
Williams, Leonard, 61, 113, 128
Wilson, S. A. K., 144
Wounds, healing of, 126
Wrinkles, cause of, 93

Yeo, B., 50

Zorten, Petrasch, centenarian, 20

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